United States Department of Agriculture

Seafood Consumption during Pregnancy and Lactation and Neurocognitive Development in the Child: A Systematic Review

2020 Dietary Guidelines Advisory Committee, Dietary Fats and Seafood Subcommittee

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Nutrition Evidence Systematic Review

Center for Nutrition Policy and Promotion

Food and Nutrition Service

U.S. Department of Agriculture

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This systematic review was conducted by the 2020 Dietary Guidelines Advisory Committee in collaboration with the Nutrition Evidence Systematic Review (NESR) team at the Center for Nutrition Policy and Promotion, Food and Nutrition Service, U.S. Department of Agriculture (USDA). All systematic reviews from the 2020 Advisory Committee Project are available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews.

Conclusion statements drawn as part of this systematic review describe the state of science related to the specific question examined. Conclusion statements do not draw implications, and should not be interpreted as dietary guidance. This portfolio provides the complete documentation for this systematic review. A summary of this review is included in the 2020 Advisory Committee's Scientific Report available at www.DietaryGuidelines.gov.

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USDA and HHS implemented a process to identify topics and scientific questions to be examined by the 2020 Dietary Guidelines Advisory Committee. The Committee conducted its review of evidence in subcommittees for discussion by the full Committee during its public meetings. The role of the Committee members involved establishing all aspects of the protocol, which presented the plan for how they would examine the scientific evidence, including the inclusion and exclusion criteria; reviewing all studies that met the criteria they set; deliberating on the body of evidence for each question; and writing and grading the conclusion statements to be included in the scientific report the 2020 Committee submitted to USDA and HHS. The NESR team with assistance from Federal Liaisons and Project Leadership, supported the Committee by facilitating, executing, and documenting the work necessary to ensure

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[i] Under contract with the Food and Nutrition Service, United States Department of Agriculture.

the reviews were completed in accordance with NESR methodology. More information about the 2020 Dietary Guidelines Advisory Committee, including the process used to identify topics and questions, can be found at www.DietaryGuidelines.gov. More information about NESR can be found at NESR.usda.gov.

The Committee and NESR staff thank USDA's Agricultural Research Service for coordinating the peer review of this systematic review, and the Federal scientist peer reviewers for their time and expertise.

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INTRODUCTION

This document describes a systematic review conducted to answer the following question: What is the relationship between seafood consumption during pregnancy and lactation and neurocognitive development in the child? This systematic review was conducted by the 2020 Dietary Guidelines Advisory Committee, supported by USDA's Nutrition Evidence Systematic Review (NESR).

More information about the 2020 Dietary Guidelines Advisory Committee is available at the following website: www.DietaryGuidelines.gov.

NESR specializes in conducting food- and nutrition-related systematic reviews using a rigorous, protocol-driven methodology. More information about NESR is available at the following website: NESR.usda.gov.

NESR's systematic review methodology involves developing a protocol, searching for and selecting studies, extracting data from and assessing the risk of bias of each included study, synthesizing the evidence, developing conclusion statements, grading the evidence underlying the conclusion statements, and recommending future research. A detailed description of the systematic reviews conducted for the 2020 Dietary Guidelines Advisory Committee, including information about methodology, is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews. In addition, starting on page 144, this document describes the final protocol as it was applied in the systematic review. A description of and rationale for modifications made to the protocol are described in the 2020 Dietary Guidelines Advisory Committee Report, Part D: Chapter 9. Dietary Fats and Seafood. The full systematic review is discussed in Chapter 2. Food, Beverage, and Nutrient Consumption during Pregnancy and Chapter 3. Food, Beverage, and Nutrient Consumption during Lactation.

List of abbreviations

Abbreviation	Full name
ADD	Attention deficit disorder
ADHD	Attention-deficit/hyperactivity disorder
ALSPAC	Avon Longitudinal Study of Parents and Children
ASD	Autism spectrum disorder
ASQ	Ages and Stages Questionnaire
BASC	Behavioral Assessment System for Children
BRIEF	Behavior Rating Inventory of Executive Functioning
BSID	Bayley Scales of Infant Development
CAST	Childhood Asperger Syndrome Test
CCCCS	Child Communication Checklist Coherence Scale
CP	Conduct problem
CPT	Continuous Performance Test
CRS-T	Conners' Rating Scale-Teachers
DAWBA	Development and Well-Being Assessment
DDST	Denver Developmental Screening Test
DGA	Dietary Guidelines for Americans
DHA	Docosahexaenoic acid
DNBC	Danish National Birth Cohort
DSA	Delayed Spatial Alternation
EAS	Emotionality, Activity, Sociability temperament traits/scale
EOP	Early-onset conduct problem
EPA	Eicosapentaenoic acid
FFQ	Food frequency questionnaire
FTII	Fagan Infant Test
GDS	Gesell Developmental Schedules

Abbreviation	Full name
HHS	Department of Health and Human Services
INMA	Spanish Childhood and Environment Project
IQ	Intelligence quotient
KBIT	Kaufman Brief Intelligence Test
KIDS	Kinder Infant Development Scale
MCDI	MacArthur Communicative Development Inventory
MDI	Mental Development Index
MoBa	Mother and Child Cohort Study
MSCA	McCarthy Scales of Children's Abilities
n-3	Omega-3
NESR	Nutrition Evidence Systematic Review
NNNS	NICU Network Neurobehavioral Scale
PCS	Prospective cohort study
PDI	Psychomotor Development Index
PPVT	Peabody Picture Vocabulary Test
PUFA	Polyunsaturated fatty acid
pVEP	Pattern-reversal visual evoked potentials
SCDC	Social and Communication Disorders Checklist
SD	Standard deviation
SDQ	Strengths and Difficulties Questionnaire
SLAS	Speech and Language Assessment Scale
SON-R	Snijders-Oomen Niet-verbale Intelligentietest Revisie (Snijders-Oomen Nonverbal Intelligence Test Revision)
SRS	Social Responsiveness Scale
U.K.	United Kingdom
U.S.	United States
USDA	United States Department of Agriculture

Abbreviation	Full name
VEXP	Visual Expectation Paradigm
WASI	Wechsler Abbreviated Scale of Intelligence
WISC	Wechsler Intelligence Scale for Children
WPPSI	Wechsler Preschool and Primary Scales of Intelligence
WRAML	Wide Range Assessment of Memory and Learning
WRAVMA	Wide Range Assessment of Visual Motor Abilities

WHAT IS THE RELATIONSHIP BETWEEN SEAFOOD CONSUMPTION DURING PREGNANCY AND LACTATION AND NEUROCOGNITIVE DEVELOPMENT IN THE CHILD?

PLAIN LANGUAGE SUMMARY

What is the question?

- The question is: What is the relationship between seafood consumption during pregnancy and lactation and neurocognitive development in the child?

What is the answer to the question?

Seafood intake during pregnancy

Developmental domains:

- Moderate evidence indicates that seafood intake during pregnancy is associated favorably with measures of cognitive development in young children.
- Limited evidence suggests that seafood intake during pregnancy may be associated favorably with measures of language and communication development in the child.
- Insufficient evidence is available to determine the relationship between seafood intake during pregnancy and movement and physical development in the child.
- Insufficient evidence is available to determine the relationship between seafood intake during pregnancy and social-emotional and behavioral development in the child.

Attention deficit disorder or attention-deficit/hyperactivity disorder-like traits or behaviors:

- Insufficient evidence is available to determine the relationship between seafood consumption during pregnancy and attention deficit disorder or attention-deficit/hyperactivity disorder-like traits or behaviors in the child.

Attention deficit disorder or attention-deficit/hyperactivity disorder diagnosis:

- No evidence is available to determine the relationship between seafood consumption during pregnancy and diagnosis of attention deficit disorder or attention-deficit/hyperactivity disorder in the child.

Autism spectrum disorder:

- Insufficient evidence is available to determine the relationship between seafood consumption during pregnancy and autism spectrum disorder-like traits or behaviors or autism spectrum disorder diagnosis in the child.

Academic performance:

- No evidence is available to determine the relationship between seafood intake during pregnancy and academic performance in the child.

Anxiety:

- No evidence is available to determine the relationship between seafood intake during pregnancy and anxiety in the child.

Depression:

- No evidence is available to determine the relationship between seafood intake during pregnancy and depression in the child.

Seafood intake during lactation

- No evidence is available to determine the relationship between maternal seafood intake during lactation and neurocognitive development in the child.

Why was this question asked?

- This important public health question was identified by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS) to be examined by the 2020 Dietary Guidelines Advisory Committee.

How was this question answered?

- The 2020 Dietary Guidelines Advisory Committee, Dietary Fats and Seafood Subcommittee conducted a systematic review to answer this question with support from the Nutrition Evidence Systematic Review (NESR) team.

What is the population of interest?

- Generally healthy pregnant and lactating women at the time of the exposure and children from birth to 18 years at the time of the outcome.

What evidence was found?

- This review identified 26 articles that met inclusion criteria.
- Most studies examined the relationship between seafood intake during pregnancy and developmental domains.
    - Seafood intake during pregnancy was predominantly related to beneficial child cognitive, and language and communication development.
    - Insufficient evidence was available to determine the relationship between seafood intake during pregnancy and child movement and physical, and social-emotional and behavioral development.
- Too few studies were available for the Committee to draw a conclusion about seafood consumption during pregnancy and attention deficit disorder (ADD), attention-deficit/hyperactivity disorder (ADHD) or autism spectrum disorder.
- Limitations include variation in methods used to assess seafood intake and developmental domain outcomes, and variations in child age at assessment.

How up-to-date is this systematic review?

- This review searched for studies from January, 2000 to October, 2019.

TECHNICAL ABSTRACT

Background

- This important public health question was identified by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS) to be examined by the 2020 Dietary Guidelines Advisory Committee.
- The 2020 Dietary Guidelines Advisory Committee, Dietary Fats and Seafood Subcommittee conducted a systematic review to answer this question with support from the Nutrition Evidence Systematic Review (NESR) team.
- The goal of this systematic review was to examine the following question: What is the relationship between seafood consumption during pregnancy and lactation and neurocognitive development in the child?

Conclusion statements and grades

Seafood intake during pregnancy

Developmental domains:

- Moderate evidence indicates that seafood intake during pregnancy is associated favorably with measures of cognitive development in young children. (Grade: Moderate)
- Limited evidence suggests that seafood intake during pregnancy may be associated favorably with measures of language and communication development in the child. (Grade: Limited)
- Insufficient evidence is available to determine the relationship between seafood intake during pregnancy and movement and physical development in the child. (Grade: Grade not assignable)
- Insufficient evidence is available to determine the relationship between seafood intake during pregnancy and social-emotional and behavioral development in the child. (Grade: Grade not assignable)

Attention deficit disorder or attention-deficit/hyperactivity disorder-like traits or behaviors:

- Insufficient evidence is available to determine the relationship between seafood consumption during pregnancy and attention deficit disorder or attention-deficit/hyperactivity disorder-like traits or behaviors in the child. (Grade: Grade not assignable)

Attention deficit disorder or attention-deficit/hyperactivity disorder diagnosis:

- No evidence is available to determine the relationship between seafood consumption during pregnancy and diagnosis of attention deficit disorder or attention-deficit/hyperactivity disorder in the child. (Grade: Grade not assignable)

Autism spectrum disorder:

- Insufficient evidence is available to determine the relationship between seafood consumption during pregnancy and autism spectrum disorder-like traits or behaviors or autism spectrum disorder diagnosis in the child. (Grade: Grade not assignable)

Academic performance:

- No evidence is available to determine the relationship between seafood intake during pregnancy and academic performance in the child. (Grade: Grade not assignable)

Anxiety:

- No evidence is available to determine the relationship between seafood intake during pregnancy and anxiety in the child. (Grade: Grade not assignable)

Depression:

- No evidence is available to determine the relationship between seafood intake during pregnancy and depression in the child. (Grade: Grade not assignable)

Seafood intake during lactation

- No evidence is available to determine the relationship between maternal seafood intake during lactation and neurocognitive development in the child. (Grade: Grade not assignable)

Methods

- A literature search was conducted using 4 databases (PubMed, Cochrane, Embase and CINAHL) to identify articles that evaluated the intervention or exposure of seafood consumption during pregnancy and lactation and the outcomes of neurocognitive development. A manual search was conducted to identify articles that may not have been included in the electronic databases searched. Articles were screened by two NESR analysts independently for inclusion based on pre-determined criteria.
- Data extraction and risk of bias assessment were conducted for each included study, and both were checked for accuracy. The Committee qualitatively synthesized the body of evidence to inform development of conclusion statements, and graded the strength of evidence using pre-established criteria for risk of bias, consistency, directness, precision, and generalizability.

Summary of the evidence

Seafood intake during pregnancy

- This review included 26 articles from 18 prospective cohort studies (PCSs) published between January 2000 and October 2019.
- The 2020 Dietary Guidelines Advisory Committee used the following seafood definition: marine animals that live in the sea and in freshwater lakes and rivers. Seafood includes fish (e.g., salmon, tuna, trout, and tilapia) and shellfish (e.g., shrimp, crab, and oysters).
- Developmental domains:
    - Evidence from 21 articles from 15 PCSs indicated predominantly beneficial associations between seafood intake during pregnancy and measures of cognitive development, including milestone achievement and intelligence, particularly in young children.
    - Evidence from 15 articles from 12 PCSs suggested beneficial associations

between seafood intake during pregnancy and measures of language and communication development. However, results were less consistent than for cognitive development. Furthermore, 8 articles assessed measures of verbal intelligence or verbal intelligence quotient (IQ), which may be less specific assessments of language and communication development.
    - Few detrimental associations between seafood intake during pregnancy and measures of child cognitive or language development were found.
    - Heterogeneity in exposure and assessment methods, and ages of children at follow-up, made it difficult to determine a relationship between seafood intake during pregnancy and movement and physical development or social-emotional and behavioral development.

- Four articles, from 3 PCSs, found inconsistent results when examining the relationship between seafood intake during pregnancy and attention deficit disorder (ADD)-like or attention-deficit/hyperactivity disorder (ADHD)-like traits or behaviors in the child, with studies reporting either null or protective associations.
- Three PCSs assessed autism spectrum disorder (ASD)-like traits or behaviors or ASD diagnosis but heterogeneity in outcome assessment methods and child age across the 3 PCSs made it difficult to determine a relationship between seafood intake during pregnancy and ASD-like traits or behaviors or ASD diagnosis.
- No studies that met inclusion criteria assessed the relationship between seafood intake during pregnancy and academic performance, anxiety or depression in the child.
- Thirteen articles accounted for maternal mercury exposure and most found that controlling for mercury exposure strengthened or had little impact on the association between seafood intake during pregnancy and developmental outcomes.
- There were limitations in the evidence:
    - Heterogeneity in seafood intake categories used to compare seafood intake levels across studies made it difficult to assess precision and compare magnitude of associations.
    - Key confounders were not consistently accounted for and there was heterogeneity in exposures, outcomes, and child age.

Seafood intake during lactation

- No studies that met inclusion criteria assessed the relationship between maternal seafood intake during lactation and neurocognitive development in the child.

FULL REVIEW

Systematic review question

What is the relationship between seafood consumption during pregnancy and lactation and neurocognitive development in the child?

Conclusion statements and grades

Seafood intake during pregnancy

Developmental domains:

- Moderate evidence indicates that seafood intake during pregnancy is associated favorably with measures of cognitive development in young children. (Grade: Moderate)
- Limited evidence suggests that seafood intake during pregnancy may be associated favorably with measures of language and communication development in the child. (Grade: Limited)
- Insufficient evidence is available to determine the relationship between seafood intake during pregnancy and movement and physical development in the child. (Grade: Grade not assignable)
- Insufficient evidence is available to determine the relationship between seafood intake during pregnancy and social-emotional and behavioral development in the child. (Grade: Grade not assignable)

Attention deficit disorder or attention-deficit/hyperactivity disorder-like traits or behaviors:

- Insufficient evidence is available to determine the relationship between seafood consumption during pregnancy and attention deficit disorder or attention-deficit/hyperactivity disorder-like traits or behaviors in the child. (Grade: Grade not assignable)

Attention deficit disorder or attention-deficit/hyperactivity disorder diagnosis:

- No evidence is available to determine the relationship between seafood consumption during pregnancy and diagnosis of attention deficit disorder or attention-deficit/hyperactivity disorder in the child. (Grade: Grade not assignable)

Autism spectrum disorder:

- Insufficient evidence is available to determine the relationship between seafood consumption during pregnancy and autism spectrum disorder-like traits or behaviors or autism spectrum disorder diagnosis in the child. (Grade: Grade not assignable)

Academic performance:

- No evidence is available to determine the relationship between seafood intake during pregnancy and academic performance in the child. (Grade: Grade not assignable)

Anxiety:

- No evidence is available to determine the relationship between seafood intake during pregnancy and anxiety in the child. (Grade: Grade not assignable)

Depression:

- No evidence is available to determine the relationship between seafood intake during pregnancy and depression in the child. (Grade: Grade not assignable)

Seafood intake during lactation

- No evidence is available to determine the relationship between maternal seafood intake during lactation and neurocognitive development in the child. (Grade: Grade not assignable)

Summary of the evidence

Seafood intake during pregnancy

- This review included 26 articles from 18 prospective cohort studies (PCSs) published between January 2000 and October 2019.[1-26]
- The 2020 Dietary Guidelines Advisory Committee used the following seafood definition: marine animals that live in the sea and in freshwater lakes and rivers. Seafood includes fish (e.g., salmon, tuna, trout, and tilapia) and shellfish (e.g., shrimp, crab, and oysters).
- Developmental domains:
    - Evidence from 21 articles from 15 PCSs indicated predominantly beneficial associations between seafood intake during pregnancy and measures of cognitive development, including milestone achievement and intelligence, particularly in young children.
    - Evidence from 15 articles from 12 PCSs suggested beneficial associations between seafood intake during pregnancy and measures of language and communication development. However, results were less consistent than for cognitive development. Furthermore, 8 articles assessed measures of verbal intelligence or verbal intelligence quotient (IQ), which may be less specific assessments of language and communication development.
    - Few detrimental associations between seafood intake during pregnancy and measures of child cognitive or language development were found.
    - Heterogeneity in exposure and assessment methods, and ages of children at follow-up, made it difficult to determine a relationship between seafood intake during pregnancy and movement and physical development or social-emotional and behavioral development.
- Four articles, from 3 PCSs, found inconsistent results when examining the relationship between seafood intake during pregnancy and attention deficit disorder (ADD)-like or attention-deficit/hyperactivity disorder (ADHD)-like traits or behaviors in the child, with studies reporting either null or protective associations.
- Three PCSs assessed autism spectrum disorder (ASD)-like traits or behaviors or ASD diagnosis but heterogeneity in outcome assessment methods and child age across the 3 PCSs made it difficult to determine a relationship between seafood intake during pregnancy and ASD-like traits or behaviors or ASD diagnosis.

- No studies that met inclusion criteria assessed the relationship between seafood intake during pregnancy and academic performance, anxiety or depression in the child.
- Thirteen articles accounted for maternal mercury exposure and most found that controlling for mercury exposure strengthened or had little impact on the association between seafood intake during pregnancy and developmental outcomes.
- There were limitations in the evidence:
    - Heterogeneity in seafood intake categories used to compare seafood intake levels across studies made it difficult to assess precision and compare magnitude of associations.
    - Key confounders were not consistently accounted for and there was heterogeneity in exposures, outcomes, and child age.

Seafood intake during lactation

- No studies that met inclusion criteria assessed the relationship between maternal seafood intake during lactation and neurocognitive development in the child.

Description of the evidence

This systematic review included 26 articles[1-26] from 18 prospective cohort studies (PCSs) that examined the relationship between seafood consumption during pregnancy and neurocognitive development in infants and children. The study and participant characteristics, including the exposure, outcome, confounders and limitations can be found in **Table 1**. No studies that met inclusion criteria examined seafood consumption during lactation and neurocognitive development in the child.

Study characteristics

Twenty-six articles from 18 PCSs were included in this systematic review.

- Avon Longitudinal Study of Parents and Children (ALSPAC) cohort: 5 articles[1,6,7,14,24]
- Project Viva: 3 articles[17-19]
- Public Health Impact of long-term, low-level, Mixed Element exposure in a susceptible population EU Sixth Framework Programme (PHIME): 2 articles[22,26]
- Spanish Childhood and Environment Project (INMA): 2 articles[10,12]
- Fifteen articles are from independent cohorts
    - Danish National Birth Cohort (DNBC)[16]
    - Generation R Study[21]
    - HOME study[25]
    - Mother and Child Cohort Study (MoBa)[23]
    - Mount Sinai Children's Environmental Health Study[4]
    - Seychelles Child Development Study[2]
    - The New Bedford Cohort[20]
    - Unnamed cohorts: 8 articles[3,5,8,9,11,13,15,22]

Country

- U.S.[4,11,17-20,25]

- Europe: U.K.,[1,5-7,14,24] Spain,[10,12,13] Italy,[3,22] and Denmark,[16] Finland,[15] The Netherlands,[21] Norway[23] and 1 cohort from Croatia, Greece, Italy, Slovenia[26]
- Asia: China,[9] and Japan[8]
- Africa: Republic of Seychelles[2]

Sample size

Study sample sizes ranged from an analytic N of 19[15] to 38,581.[23]

- <200 participants: 6 articles[3,4,8,11,15,19]
- 200 to 700 participants: 9 articles[2,5,9,13,17,20,22,24,25]
- 1,000 to 8,000 participants: 9 articles[1,6,7,10,12,14,18,21,26]
- 25,446 and 38,581 participants: 2 articles[16,23]

Demographics

- Pregnant women included in the studies had a mean age of approximately 30 years, ranging from 16 years to 47 years.
- The majority of participants completed high school and a large proportion had completed some college or a college degree.
- Eleven articles reported race and ethnicity:
  - Two articles from the ALSPAC cohort included approximately 98% White participants.[7,14]
  - Seven articles from studies conducted in the U.S. reported more racial or ethnic diversity.
    - Six articles (3 from Project Viva) included 63 to 82% White or Caucasian, 6 to 30% Black, African American, or other participants.[11,17-20,25]
    - One article included 50% Hispanic, 32% African American or other, and 19% White participants.[4]
  - One study from the Netherlands included approximately 59% Dutch and 41% non-Dutch participants.[21]
  - One study conducted in the U.K. (separate from the ALSPAC cohort) included 100% White or Caucasian participants.[5]
- Seventeen articles provided some measure of parity, with nulliparous or primiparous individuals ranging from 36% to 72%. One study exclusively enrolled primiparous women.[4]
- Among offspring, the percentages of girls and boys were balanced.

Exposures

All articles assessed maternal seafood intake during pregnancy and no articles assessed seafood exposure during lactation.

- Total maternal fish and shellfish intake: 15 articles[3,5,7-14,17-23,25,26]
- Total maternal fish intake (no shellfish): seven articles[1,2,13,15-17,24]
- Oily fish intake only: 3 articles[5,6,24]
- White fish intake only: 2 articles[6,24]
- Large fatty fish, smaller fatty fish, and lean fish intake analyzed separately: 1 article[10]
- Canned fish intake: 3 articles on canned fish,[4,6,24] 1 on canned seafood,[3] and 1 on

canned tuna fish[17]

- Shellfish intake: 4 articles[6,10,13,24]

Method of exposure measurement

- Timing of assessment
    - Assessed seafood intake during pregnancy at one time point: 21 articles
        - Second trimester (approximately 13 to 27 weeks gestation), 5 articles: 14 weeks gestation,[21] 22 weeks gestation,[23] 25 weeks gestation,[16] 26-28 weeks gestation,[17,19] and two weeks prior to third trimester[15]
        - Third trimester (approximately 28 weeks gestation to birth), 8 articles: 28 weeks gestation,[2] 32 weeks gestation,[1,6,7,14,24] third trimester[4]
        - Post-partum (intake during pregnancy assessed post-delivery), 7 articles: 5 articles soon after delivery,[9,11,20,22,26] 1 article at 2-3 months postpartum,[3] and 1 article at 3 months postpartum[13]
        - One article did not report the timing of assessment[8]
    - Assessed seafood intake during pregnancy at 2 time points: 5 articles
        - Between 10 and 13 and between 28 and 32 weeks gestation[10,12]
        - At 15 and 32 weeks gestation[5]
        - At 16 weeks gestation and 5 weeks post-partum[25]
        - At 28 week gestation and post delivery[18]

- Type of assessment tool
    - Food frequency questionnaire (FFQ): 19 articles
        - Validated against blood biomarkers and/or food diaries: 15 articles[1,6,7,10,12,14,16-19,21-24,26]
        - No information provided on validity: 4 articles[3,5,13,20]
    - Study questionnaire developed for the study: 6 articles
        - No information provided on validity[4,8,9,11,15,25]
    - Dietary recall and food use questionnaire: 1 article
        - Food use questionnaire (completed between 26 and 28 weeks gestation) and a 4-day food diary completed at 28 weeks gestation[2]

Contextual factors

Several contextual factors related to seafood consumption were identified *a priori* to consider during synthesis. These included nutrients in seafood (e.g., omega-3 [n-3] polyunsaturated fatty acids [PUFAs], iodine, selenium, iron, fish protein, and vitamin D), environmental contaminants frequently found in seafood (e.g., mercury), blood and human milk biomarkers of seafood intake, and infant feeding practices.

- Environmental contaminants – mercury exposure was addressed in analysis of 13 articles
    - Developmental domains: 13 articles accounted for mercury in some or all analyses[1-3,10-12,17-20,22,23,25]
    - Attention deficit disorder (ADD)/Attention-deficit/hyperactivity disorder (ADHD)-like behaviors or traits: 1 article concurrently considered seafood and mercury intake[20]

- Seafood nutrients - maternal biomarkers of seafood intake was addressed in 7 articles pertaining to developmental domains
    - Docosahexaenoic acid (DHA)[2,15,17,22,24]

    - Eicosapentaenoic acid (EPA)[15,17,22]
    - DHA and EPA combined[18]
    - Arachidonic acid (AA)[2]
    - Total n-3[22]
    - Selenium[18,23]

- Infant feeding practices
    - Eighteen articles reported baseline data on infant feeding practices, but variation in reporting prevents summarization
    - Two articles stratified results by breast feeding duration[13,16] and 1 article provided a sub-analysis in women who never breastfed[24]
    - Many studies controlled for breastfeeding in analysis

Outcomes

Articles included in this review assessed neurocognitive development, ADD or ADHD-like behaviors or traits, ASD-like behaviors or traits, and ASD diagnosis. No studies assessed child academic performance, anxiety, or depression outcomes. Many studies used a combination of tools, scales and indicators to measure neurocognitive development. Some neurocognitive development tools included subscales to measure hyperactivity, distractibility, inattentive and hyperactive-impulsive behavior. These outcomes are described with ADD/ADHD-like behaviors or traits. Thus, indicators may be listed with both neurocognitive developmental domains and ADD/ADHD-related outcomes.

Methods of neurocognitive developmental domain outcome assessment

Neurocognitive developmental outcomes were examined by domain including cognitive development (including intelligence quotient [IQ]), language and communication development, movement and physical development, and social-emotional and behavioral development. Most of the neurocognitive assessment tools administered in the included articles are widely used and have been validated for use in certain populations, such as the Bayley Scales of Infant Development (BSID), Wechsler scales of intelligence, the Conners' Rating Scale - Teachers (CRS-T), and the Fagan Test of Infant Intelligence (FTII). However, the validity and reliability of any assessment of neurocognitive development when used in an individual study depends on a variety of factors such as the validity of an assessment for the particular population under examination, appropriate administration of the assessment, and training of study personnel administering the assessment; this detailed information was not provided in all studies. Several articles reported that study personnel were trained to administer the neurocognitive assessments.[2,3,7,9,10,12,13,15,17-19,22,25,26] Some studies used assessments that were adapted or developed for use in the study, making it more difficult to evaluate the validity or reliability of those particular measures.[1,7,16] One article reported that the neurocognitive assessment method (stereopsis testing) utilized had only moderately reliable repeatability.[24] Below is a list of tools, scales, and indicators used to measure neurocognitive development. Because many tools assess multiple domains of development, some tools are listed across a variety of neurocognitive developmental domains and may also be included with ADD/ADHD- and ASD-related outcomes.

- Cognitive development (including IQ) assessment measures and age at assessment (20 articles)
    - ALSPAC-adapted Denver Developmental Screening Test (DDST) at 6,18, 30, and 42 months[7]; at 18 months[1]
    - A-not-B Test at 25 months[2]
    - Book-format random dot stereoacuity test at 3.5 years[24]
    - Bayley Scales of Infant Development (BSID) at 14 months[10,12]
    - Bayley Scales of Infant Development-II (BSID-II) at 9 and 30 months[2]; at 12, 24, and 36 months[11]
    - Bayley Scales of Infant Development-III (BSID-III) at 18 months[22,26]
    - Investigator developed infant and child milestone assessments at 6 and 18 months[16]
    - Neurobehavioral Evaluation System 2 Continuous Performance Test (CPT) at 8 years[20]
    - Delayed Spatial Alternation (DSA) at 25 months[2]
    - Kaufman Brief Intelligence Test (KBIT-II) at 6-11 years[18]
    - Kinder Infant Development Scale (KIDS) at 18 months[8]
    - McCarthy Scales of Children's Abilities (MSCA) at 4 years[13]; at 5 years[10]
    - Pattern-reversal visual evoked potentials (pVEP) recordings at 2 years[15]
    - Snijders-Oomen Niet-verbale Intelligentietest – Revisie (SON-R) (Snijders-Oomen Nonverbal Intelligence Test Revision) at 6 years[21]
    - Visual Expectation Paradigm (VEXP) at 5 and 9 months[2]
    - Visual recognition memory at 5 and 9 months using Fagan Test of Infant Intelligence (FTII)[2]; at 6.5 months[19]
    - Wechsler Abbreviated Scale of Intelligence (WASI) at 9 years[5]
    - Wechsler Intelligence Scale for Children-III (WISC-III) at 7 years[3]; at 8 years[7,20]
    - Wechsler Intelligence Scale for Children-IV (WISC-IV) at 7-9 years[4]
    - Wechsler Preschool and Primary Scales of Intelligence-III (WPPSI-III) at 6 years[4]
    - Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) at 48 months[11]
    - Wide Range Assessment of Memory and Learning (WRAML) at 6-11 years[18]
    - Wide Range Assessment of Visual Motor Abilities (WRAVMA) at 3 years[17]; at ~6-11 years[18]

- Language and communication development assessment measures and age at assessment (14 articles)
    - ALSPAC-adapted DDST at 6, 18, 30 and 42 months[7]; at 18 months[1]
    - ALSPAC-adapted MacArthur Communicative Development Inventory (MCDI) at 15 months[1]
    - Norwegian Ages and Stages Questionnaire (ASQ) at 5 years[23]
    - BSID-III at 18 months[22,26]
    - Chinese Pediatric Association-adapted Gesell Developmental Schedules (GDS) at 1 years[9]
    - KBIT-II at 6-11 years[18]
    - KIDS at 18 months[8]
    - Twenty Statements about Language-Related Difficulties List (Language 20)

at 5 years[23]
  - MSCA at 4 years[13]; at 5 years[10]
  - Peabody Picture Vocabulary Test (PPVT) at 3 years[17]
  - Speech and Language Assessment Scale (SLAS) at 5 years[23]
  - WASI at 9 years[5]
  - WISC-III at 7 years[3]; at 8 years[7]
  - WISC-IV at 7-9 years[4]
  - WPPSI-III at 6 years[4]
  - WPPSI-R at 48 months[11]

- Movement and physical development assessment measures and age at assessment (13 articles)
  - ALSPAC-adapted DDST at 6, 18, 30, and 42 months[7]
  - BSID at 14 months[10,12]
  - BSID-II at 9 and 30 months[2]; at 12, 24, and 36 months[11]
  - BSID-III at 18 months[22,26]
  - Chinese Pediatric Association-adapted GDS at 1 year[9]
  - Investigator developed infant and child milestone assessments at 6 and 18 months[16]
  - KIDS at 18 months[8]
  - MSCA at 4 years[13]; at 5 years[10]
  - NICU Network Neurobehavioral Scale (NNNS) at 5 weeks[25]
  - WRAVMA at 3 years[16,17]; at 6-11 years[18]

- Social-emotional and behavioral development assessment measures and age at assessment (nine articles)
  - ALSPAC-adapted DDST at 6, 18, 30 and 42 months[7]; at 18 months[1]
  - ALSPAC-adapted MCDI at 15 months[1]
  - Behavioral Assessment System for Children (BASC) at 4-9 years[4]
  - Behavior Rating Inventory of Executive Functioning (BRIEF) at 4-9 years[4]
  - BSID-III at 18 months[22]
  - Chinese Pediatric Association-adapted GDS at 1 years[9]
  - KIDS at 18 months[8]
  - NNNS at 5 weeks[25]
  - Strengths and Difficulties Questionnaire (SDQ) at 4-10 and 12-13 years[14]; at 7 years[7]; at 9 years[5]

- ADD- or ADHD-like traits or behaviors assessment measures and age at assessment (four articles)
  - Conners' Rating Scale-Teachers (CRS-T) at 8 years[20]
  - SDQ at 4-13 years[14]; at 7 years[7]; at 9 years[5]

- ASD-like traits or behaviors assessment measures and age at assessment (three articles)
  - ALSPAC derived measure of repetitive behavior at 5 years[6]
  - Childhood Asperger Syndrome Test (CAST) at 5 years[10]
  - Child Communication Checklist Coherence Scale (CCCCS): Coherent speech at 9 years[6]

    - Emotionality, Activity, Sociability (EAS) temperament traits/scale: Sociability at 3 years[6]
    - Social and Communication Disorders Checklist (SCDC): Social communication at 7 years[6]
    - Social Responsiveness Scale (SRS) at 6 years[21]

- ASD diagnosis assessment method and age at assessment (one article)
    - Diagnosis of ASD by 11 years identified via educational records, maternal/parental report, classification as "Pervasive Development Disorder" from DAWBA (Development and Well-Being Assessment)[6]

Evidence synthesis

Neurocognitive developmental domain outcomes

Seafood intake during pregnancy and neurocognitive development were assessed by domain:

- Cognitive development, including IQ and composite intelligence measures
- Language and communication development including verbal IQ and verbal intelligence
- Movement and physical development (e.g., fine or gross motor development, psychomotor development)
- Social-emotional and behavioral development

Results from the included studies are described in **Table 2** (developmental domains) and **Table 3** (ADD and ADHD) and a summary of risk of bias assessment is found in **Table 4**.

Seafood intake during pregnancy and child cognitive development

Twenty-one articles from 15 PCSs examined the relationship between maternal seafood intake during pregnancy and cognitive development in children 5 months to 11 years and IQ or composite intelligence measures in children 4 to 11 years of age. Articles were categorized by age group (less than and greater than four years) and type of cognitive outcome (cognitive development and intelligence) for analysis.

Cognitive development and infant and toddler development (Under 4 years of age)

Thirteen articles from nine PCSs examined the relationship between seafood consumption during pregnancy and cognitive development in infants and toddlers ages 5 months to 4 years. Seven articles from six PCSs reported a beneficial association between maternal seafood intake and cognitive development in children 6 months to 3.5 years, examined using a variety of assessment methods.[1,8,10,16,17,19,24] Six articles from 5 PCSs reported no association between seafood consumption during pregnancy and cognitive development in infants and toddlers 4 years and younger.[2,11,12,15,22,26]

One large study from the DNBC (N=25,446) examined maternal fish intake during the second trimester (assessed at 25 weeks gestation) using a validated FFQ and its relationship to the achievement of developmental milestones at 6 and 18 months of age using an investigator-developed maternal report tool.[16] Average maternal fish intake was 26.6 grams per day (6.6 ounces per day; SD=22.7 grams per day; 186.2 grams per week) and the most frequently consumed fish species included cod, plaice, salmon, herring, mackerel (85% of total seafood intake in DNBC).[16] Higher prenatal fish intake was significantly associated with better total development and social/cognitive developmental subscale scores at 6 and 18 months of age, when fish intake was modeled continuously, categorically by quintiles, and by servings per week (0 vs 1-2 servings per week; 0 vs ≥3 servings per week). Specifically, significant associations were found when comparing the highest quintiles to the lowest quintiles at 6 months (N=28,958). For example, quintile 4 (Median=226.1 grams [8 ounces] per week) vs quintile 1 (Median=41.3 grams [1.5 ounces] per week) and quintile 5 (Median=355.6 grams or 12.5 ounces per week) vs quintile 1 of fish intake were associated with higher scores on the total development scale and social/cognitive development subscale.[16] Similar findings were observed at 18 months; in addition, Q3 (Median=155.4 grams [5.5 ounces] per week) vs Q1 (Median=41.3 grams [1.5 ounces] per week) intake was significantly associated with higher total development and social/cognitive development scores.[16] These associations were similar among those breastfed ≤6 months and >6 months. Data on maternal mercury exposure were not available in this cohort.

Two articles from the Project Viva cohort in the U.S. examined maternal seafood intake during the second trimester and cognitive development in infancy (N=135)[19] and toddlerhood (N=341).[17] Mean maternal seafood intake was 1.2 servings per week[19] and 1.5 servings per week.[17] Servings sizes were 3-4 ounces of canned tuna fish, "1 serving" of shrimp, lobster, scallops or clams, 3-5 ounces of "dark meat fish" and other fish.[17,19] Infant visual recognition memory at 6.5 months was assessed using a novelty preference test[19] and toddler cognitive development and visual-spatial subscale were assessed with the WRAVMA at 3 years.[17] Higher seafood intake during pregnancy was associated with greater visual recognition memory at 6.5 months in the child – for each additional weekly serving of seafood, child visual recognition memory score (percent novelty preference) was 4.0 points and 2.8 points higher with and without adjustment for maternal hair mercury, respectively.[19] Maternal seafood intake >2 servings per week, but not ≤2 servings per week, during pregnancy was associated with better child development at 3 years, compared to no consumption of seafood.[17] Similar to the results from infancy, this association was strengthened after adjusting for maternal erythrocyte mercury. Canned tuna intake (never vs >2 servings per week) and fish intake other than shellfish during pregnancy were also positively associated with WRAVMA total score in the child.[17] No association between maternal seafood intake during pregnancy and child performance on the WRAVMA visual spatial subscale was detected.

Two prospective cohort studies from the ALSPAC cohort reported significant associations between maternal fish intake during pregnancy (N~443) and preschool child cognitive development, using the ALSPAC-adapted DDST at 18 months (N=7116)[1] and a stereoacuity test at 3.5 years (N~443).[24] At 18 months, there was a significant positive trend between frequency of fish intake during pregnancy, assessed at 32 weeks (from rarely/never to 4+ meals per week), and mean raw total scores on the ALSPAC-adapted DDST.[1] Additionally, there was a significant negative trend between frequency of fish intake during pregnancy and odds of scoring at the lowest 15th percentile.[1] The results were similar when adjusted for cord mercury in a subset of participants (N=1054), although these data were not reported. At 3.5 years, stereoacuity was assessed using an orthoptist administered book-format random dot stereoacuity test in a smaller subset of the ALSPAC cohort.[24] Oily fish intake, but not white fish or shellfish intake, was significantly associated with achievement of foveal stereoacuity (i.e., maturation to adult or high-grade levels) at 3.5 years; no adjusted analyses were conducted for total fish intake. Maternal mercury exposure was not adjusted for in analyses and results were not impacted by infant feeding mode.

One article from the Spanish INMA cohort, with a mean fish intake of approximately 498 grams or 17.6 ounces per week, (N=1982) examined the association between seafood, large fatty fish, small fatty fish, lean fish, and shellfish intake separately during the first and third trimesters and cognitive outcomes.[10] Outcomes were assessed using the BSID Mental Development Index (MDI) scores at 14 months of age. When seafood intake was modeled continuously, no association with MDI scores was detected.[10] However, when seafood intake was modeled categorically by quintiles, beneficial associations with MDI scores were detected when comparing the second (Median=338 grams [11.9 ounces] per week of seafood) vs first (Median=195 grams [6.9 ounces] per week of seafood) and fourth (Median=600 grams [21.2 ounces] per week of seafood) vs first quintiles of intake.[10] When specific types of seafood were examined, a benefit of small fatty fish intake (highest vs lowest quartile) was detected; however, no associations between large fatty fish, lean fish, or shellfish intake and MDI scores were observed.[10]

In a small Japanese cohort (N=88), frequent seafood consumption, compared to less frequent consumption, was significantly associated with greater Development Quotient scores, assessed using the KIDS at 18 months.[8] This study did not specify the cutoff for the dichotomous seafood exposure variable and did not control for maternal mercury exposure.[8]

Six studies from five different countries detected no positive associations between seafood intake and cognitive development during infancy and toddlerhood.[2,11,12,15,22,26] Five of these studies utilized a version of BSID cognitive assessment tools. The units of the seafood exposure measure varied across these studies, including times per week, servings per week, and grams per day or week.

Specifically, there was no association between prenatal seafood intake and BSID MDI scores at 14 months in one analysis of the INMA cohort where maternal mercury exposure was the focus of the analyses.[12] This was similar to the results from the INMA cohort in which no association was observed between prenatal seafood intake modeled continuously and MDI scores.[10] In a New York City cohort (N=151), designed primarily to examine environmental contaminants, 71.5% of participants reported consuming seafood during pregnancy. No maternal seafood consumption during pregnancy, compared to any seafood consumption, was not associated with BSID-II MDI scores at 12, 24, and 36 months of age.[11] Two studies from the PHIME cohort (N=606[22] and N=1308)[26] reported no association between overall seafood intake during pregnancy and BSID-III cognitive scores at 18 months. Average total seafood intake in these studies was 2.33 (SD=1.71), 150 gram (5.3 ounce) servings per week[22] and 1.4 (SD=1.2) servings per week.[26] Two studies adjusted for maternal mercury in all analyses.[11,22] The Seychelles Child Development Study cohort (N=229), with a relatively high mean maternal fish intake of 537 grams (18.9 ounces) per week, found no association between maternal fish intake at 28 weeks gestation and BSID-II MDI scores at 9 and 30 months.[2] In addition to the BSID-II, no significant association was found between maternal fish intake at 28 weeks gestation and infant novelty preference at 5 and 9 months, visual recognition memory at 5 and 9 months, and child planning, inhibition, attention and working memory at 25 months.[2] Results of analyses with and without adjustment for maternal mercury exposure were similar. Finally, maternal fish intake was not significantly associated with pVEP amplitude or latency at 2 years of age in a convenience sample of participants (N=19; attrition rate: 92%) from an existing Finnish randomized control trial; however, it is likely that the study was underpowered and the attrition rate was very high.[15] Maternal mercury exposure was not accounted for in the analysis.

Two studies conducted analyses by breastfeeding status.[16,24] One study found a significant association between fish intake at 25 weeks gestation and milestone achievement at 18 months of age for both children breastfed ≤6 months or >6 months.[16] Although the directionality of the results was the same as when all participants were included, the other study did not detect a statistically significant association between oily fish intake during pregnancy and foveal stereoacuity at 3.5 years in a small subsample of children who were never breastfed (101 out of 443 children).[24]

Several articles assessed the influence of maternal mercury exposure on the relationship between prenatal seafood intake and child cognitive development, some conducting analyses both adjusted and unadjusted for mercury exposure. In these studies, adjusting for mercury exposure generally strengthened the relationship between prenatal seafood intake and child cognition[17,19] or had little impact on the association.[1,2,18] In some cases, information on mercury exposure was only available for a subset of the primary analytic sample.[1,18]

Cognitive development in childhood (4 years of age and older)

Five studies from independent PCSs examined the association between maternal seafood intake and cognitive development in early and mid-childhood. Four of these studies detected beneficial associations among children 4 to 11 years of age,[4,10,13,18] with two of these four studies also finding detrimental associations.[13,18] However, the results from one study were predominantly null,[18] and detrimental associations in the second study were primarily limited to squid and shellfish intake.[13]

Two studies conducted in separate Spanish cohorts found positive inverse U-shaped associations between seafood intake during pregnancy and subscales of the MSCA at 4 years[13] and 5 year of age.[10] Among children who were breastfed for less than 6 months (N=234), prenatal fish intake of 2-3 times per week, but not >3 times per week, was associated with better performance on MSCA perceptual-performance, memory, and numeric subscales at 4 years of age.[13] Among children breastfed for greater than 6 months (N=143), there was a negative association between fish intake >3 times per week, compared to <1 time per week, and the memory subscale. In addition, prenatal intake of squid and shellfish (>1 time per week compared to <0.5 time per week) was associated with worse performance on the perceptual performance and numeric subscales.[13] In the INMA cohort, (N=1683) positive associations were detected between first trimester seafood intake and child performance at 5 years of age.[10] Specifically, beneficial associations were found on memory, quantitative, executive function, and perceptual-performance subscales, with benefits predominantly seen at the second through fourth quintiles of intake (Median=338 grams [11.9 ounces] per week and Median=600 grams [21.2 ounces] per week, respectively) compared to the first quintile of intake (Median=195 grams or 6.9 ounces per week). No association between third trimester seafood intake and child scores on the perceptual-performance subscale was detected (no other subscales were examined). Although types of seafood and performance on MSCA subscales were not examined for first trimester intake, beneficial associations between maternal large fatty fish intake, but not small fatty fish, lean fish, or shellfish intake, and child scores on the perceptual-performance subscale were detected.[10] Neither study adjusted for maternal mercury exposure in analyses.[10,13]

In contrast to results from the Project Viva cohort during infancy and at 3 years of age, a Project Viva cohort, which assess outcomes in children 6 to 11 years of age (Mean=7.7 years), did not detect a consistent beneficial association between prenatal seafood intake (N=1068) and child cognitive functioning, specifically in picture memory and design memory subtests.[18] Mid-pregnancy seafood intake (>0-<3 servings per week vs 0 servings per week) was associated with worse performance on the WRAML total summary score when testing group differences.[18] Late-pregnancy seafood intake was associated with lower risk of being in the lowest quartile of WRAML summary scores, for those who consumed >0-<3 servings per week or >3 servings per week compared to no consumption.[18] However, no association was seen when WRAML visual memory summary scores were modeled continuously or when late-pregnancy seafood intake was modeled continuously. Because previous studies from the Project Viva cohort had smaller sample sizes than this study, analyses were repeated in this subgroup with early childhood data and the findings were similarly null.

A study conducted in an ethnically diverse cohort from New York City (N=162), assessed maternal canned fish intake during pregnancy with a single question and analyzed dichotomously (<1 time per week versus ≥1 time per week).[4] The type of canned fish was not assessed. The majority of women (87%) consumed canned fish <1 time per week. Principal component analysis identified two cognitive factors based on scales from the WPPSI-III at 6 years and WISC-IV at 7-9 years: perceptual reasoning and processing speed. Children of mothers who consumed canned fish at least once a week scored half a standard deviation higher on the perceptual reasoning factor, but there was no association with the processing speed factor.[4] No adjustment for maternal mercury exposure was made.

The remaining study, conducted in the U.S., did not observe an association between seafood intake and child cognitive development.[20] This study from the New Bedford Cohort, assessed the associations between prenatal mercury exposure and seafood intake (N=421) and child attention-related cognitive performance at 8 years of age.[20] Prenatal seafood consumption (Mean=3.7 servings per week, SD=3.9) was not associated with performance on the CPT or WISC-III processing speed and freedom from distractibility scores. The serving size of fish was not defined in this study.[20]

Intelligence assessments in childhood (4 years and older)

Eight articles from individual PCSs assessed maternal seafood intake and its relationship to child performance on composite measures of intelligence or

IQ.[3,5,7,10,11,13,18,21] Because of the broader scope of these assessments of intelligence and IQ, they are reported separately from assessments or subscales which address more specific cognitive domains (Note: measures of verbal intelligence or verbal IQ are reported in the language and communication development section). Of these eight studies, five reported beneficial associations with maternal seafood intake during pregnancy.[5,7,10,11,13]

One ALSPAC cohort study, assessed the relationship between maternal seafood intake during pregnancy (N=5150; Mean=235 gram [8.3 ounces] per week, SD=202) and child full scale IQ and performance IQ at 8 years of age as measured by the WISC-III. A significant trend was detected for full scale IQ such that the odds of having a low score (lowest quartile) decreased as maternal seafood intake increased from 0 grams to 1-340 grams (0-12.0 ounces) and >340 grams (>12 ounces) per week.[7] However, individual comparisons between these intake groups were not significant. Maternal seafood intake was not associated with odds of having a low score for performance IQ.

A separate cohort from the U.K. examined the association between seafood and oily fish intake in early or late pregnancy and WASI full-scale IQ and performance IQ scores at 9 years of age.[5] Total seafood intake during early pregnancy was not associated with either child full-scale IQ or performance IQ for both seafood intake at early and late pregnancy. However, total seafood intake in late pregnancy was associated with higher full-scale IQ scores among children. When comparing <1 time per week and 1-2 times per week to never; eating seafood 3 or more times a week was not significantly associated with higher IQ. When oily fish intake during early and late pregnancy was assessed, no association with full-scale IQ or performance IQ scores for either period was detected.

One U.S. cohort (N=107) focused on prenatal mercury exposure in children whose mothers lived in the New York City area and were pregnant during the World Trade Center attack.[11] A significant positive association was observed between seafood consumption during pregnancy (assessed via questionnaire and analyzed as a dichotomized variable, i.e., any or none) and child full-scale IQ, but not performance IQ at 4 years of age as assessed by the WPPSI-R, when controlled for mercury.[11] Seventy-two percent of women reported eating seafood during pregnancy.

Finally, two cohort studies conducted in Spain reported inverse U-shaped associations between prenatal seafood intake and MSCA general cognitive scores at 4 year of age[13] and 5 years of age.[10] In the INMA cohort, a beneficial association was reported between first trimester total seafood intake (N=1,589) and child MSCA general cognitive scale scores.[10] A specific benefit was observed when comparing the third and fourth quintiles of intake (Median intakes 461 grams [16.3 ounces] per week and 600 grams [21.2 ounces] per week, respectively) to the first quintile of intake (Median=195 grams [6.9 ounces] per week). Seafood intake during the third trimester was not associated with general cognitive scale scores. When types of fish were considered, a beneficial association between both first trimester large fatty fish intake (modeled categorically) and third trimester large fatty fish intake (modeled continuously) and MSCA general cognitive scale scores were detected. Additionally, first trimester lean fish intake was associated with higher MSCA general cognitive scores when comparing the fourth quintile (Median=382 grams [13.5 ounces] per week) to the first quintile of intake (Median=90 grams [3.2 ounces] per week); no associations were detected when comparing third trimester intake of lean fish intake. Small fatty fish intake and shellfish intake during both the first and third trimesters were not associated with MSCA general cognitive scale scores. In a slightly smaller subsample with cord blood mercury data available, analyses on total seafood intake, large fatty fish intake and lean fish intake, adjusted for cord blood mercury, returned null results. In the other Spanish cohort (N=392), no association was found between total seafood intake during pregnancy and performance on the MSCA general cognitive scale at 4 years of age.[13] However, when the type of seafood was considered for children breastfed less than 6 months (N=234), a positive association was found between the reference fish intake (< 1 time per week) versus an intake of >2-3 times per week, but no association was found with an intake greater than 3 times per week or intake of 1 to 2 times per week. In contrast to the results for fish, a detrimental association between shellfish and squid intake and MSCA general cognitive scale scores was detected, with intake <0.5 times per week compared to >1 time per week (N=155), but not at the 0.5 to 1 time per week intake level.

Three of the eight studies that assessed composite measures of intelligence or IQ did not detect any associations with prenatal seafood intake.[3,18,21] One cohort (N=154) utilized the WISC-III to evaluate the association between fish intake during pregnancy (assessed 2 to 3 months after delivery using a FFQ) and full-scale IQ and performance IQ scores in 7 year old Italian children.[3] Both fresh fish intake and canned fish intake during pregnancy were not associated with full-scale IQ or performance IQ. The Dutch Generation R cohort (N=3,802) evaluated the association between maternal seafood intake in early pregnancy (assessed with a validated FFQ at 14 weeks gestation; mean=11.5 grams [0.41 ounces] per day) and child nonverbal IQ score at 6 years of age, assessed with the Dutch SON-R.[21] No associations between maternal seafood intake and child nonverbal IQ were detected.[21] Finally, in a study from the Project Viva cohort (N=1068) examined the relationship between maternal seafood intake during both early and late pregnancy and child nonverbal IQ scores on the KBIT-II at 6-11 years of age (Mean= 7.7 years), finding no associations.[18]

Summary

All but two articles[7,10] in this body of evidence had a serious risk of bias due to confounding, failing to account or adjust for at least one key confounder. Fewer than half of the articles accounted for most key confounders. Among the key confounders, non-fish exposure to n-3 PUFA, race or ethnicity, and maternal anthropometrics were less commonly considered. There were limitations to the measurement of the exposure, including exposure assessment tools with no information on validation,[4,8,11,15] unknown periods of seafood intake assessments,[8] unknown cut points used to determine exposure groups,[8,11] and assessments of limited types of fish, such as only canned fish intake.[4] Eleven articles considered the potential impact of maternal mercury exposure in their analysis,[1-3,10-12,17-20,22] whereas the remaining articles did not account for maternal mercury exposure in analysis. Several studies were designed to evaluate environmental contaminants; therefore, analysis of seafood intake and cognitive development were less direct.[2,4,8,11,26] A wide range of commonly used and validated assessment scales and indices were used to assess milestone achievement and cognitive development and intelligence.

Thirteen articles from nine PCSs examined the relationship between seafood consumption during pregnancy and cognitive development in infants and toddlers ages 5 months to less than 4 years.[1,2,8,10,12,15-17,19,24,26] Seven articles from studies conducted in the U.S. (3 articles from Project Viva), the U.K. (2 articles from ALSPAC), Japan and Spain, ranging in size from 88 to 25,446 participants, reported a beneficial association between total seafood intake or oily fish intake during pregnancy and cognitive development in children 6 months to 3.5 years.[1,8,10,16,17,19,22,24] Six articles from studies conducted in Italy, Croatia, Greece, Italy and Slovenia, the U.S., Spain, the Seychelles, and the Netherlands reported a null association.[2,11,12,15,22,26] No study found a detrimental association between seafood intake during pregnancy and cognitive outcomes in infants and toddlers less than 4 years of age. In general, statistically significant associations were found when seafood intake was analyzed categorically,[1,10,16,17,24] but not when analyzed continuously.[2,10,12,22,24] There were two exceptions: One study with a very large sample size found a significant, beneficial association when analyzed continuously and categorically.[16] Another study found a statistically significant beneficial association when intake data were modelled continuously, but not when analyzed categorically.[19] However, there were only nine participants in one of the two categories and the direction of results did not change.[19]

Four of five articles from studies conducted in Spain and the U.S. detected beneficial associations in children 4 to 11 years of age[4,10,13,18]; however, results from the Project Viva cohort were predominantly considered null.[18] Two studies conducted in Spain found inverse U-shaped associations between seafood intake during pregnancy and subscales of the MSCA at 4 years and 5 year of age.[10,13] One study conducted in the U.S. found a beneficial association between canned fish intake during pregnancy and cognitive development at 6 to 11 years.[4] This study assessed canned fish intake only, with low consumption reported (87% consumed canned fish <1 per week), and the risk of bias was high due to confounding and potential misclassification of the exposure; therefore, results were considered with caution.[4] A Spanish cohort found beneficial associations for fish intake and detected a detrimental association between maternal shellfish and squid intake and aspects of cognitive development at 4 years of age.[13] The Project Viva study examined prenatal seafood intake and child cognitive development at 6 to 11 years of age and found predominantly null results, and one beneficial and one detrimental finding.[18] Eight articles from studies conducted in the U.S. and Europe assessed maternal seafood intake during pregnancy and child performance on composite measures of IQ and intelligence (full scale IQ and non-verbal IQ) in children 4 to 11 years of age.[3,5,7,10,11,13,18,21] Five of six studies that assessed full scale IQ or general cognitive scale score reported a beneficial association with maternal seafood intake during pregnancy, with some evidence of an inverse-U relationship in cohorts with higher average intake levels.[5,7,10,11,13] Results from a New York City cohort were interpreted with caution due to concerns regarding risk of bias described earlier.[11]

No association between prenatal seafood intake and child performance/non-verbal IQ were detected in the six studies that assessed it.[3,5,7,11,18,21] A Spanish cohort found that maternal shellfish and squid intake during pregnancy was negatively associated with perceptual performance subscale scores in a subsample of children breastfed greater than 6 months.[13] Variation in seafood assessment (timing, type, and analysis method) made it difficult to detect trends in the evidence.

Twenty-one articles examined the relationship between maternal seafood intake during pregnancy and cognitive development in children 5 months to 11 years and IQ or composite intelligence measures in children 4 to 11 years of age. Overall, there was evidence of beneficial associations between prenatal seafood intake and child cognitive development, particularly among young children; however, results were moderately inconsistent and study heterogeneity makes quantification difficult.

Seafood intake during pregnancy and child language and communication development

Fifteen articles from twelve PCSs examined the relationship between seafood intake during pregnancy and language and communication development in the child.[1,7-9,17,22,23,26] Eight articles used assessment measures that produce verbal intelligence or verbal IQ scores, which are less specific to language and communication development but rely heavily on these skills.[3-5,7,10,11,13,18] Eight articles used assessment measures and scales specific to language and communication development.[1,7-9,17,22,23,26]

Among the eight articles that used specific measures of child language and communication development, three detected a beneficial association with maternal seafood intake during pregnancy.[1,7,23] Two of these articles were from the ALSPAC cohort.[1,7] One study examined the association between prenatal fish intake (assessed at 32 weeks gestation) and the child's language score on ALSPAC-adaptations of the MCDI and DDST at 15 months (N=7329) and 18 months of age (N~7100), respectively.[1] Whether the ALSPAC-adaptations of the MCDI and DDST were validated was not reported. At 15 months of age, greater maternal fish intake during pregnancy was associated with better MCDI vocabulary comprehension scores, particularly at intakes >1 meal per week; at 18 months, similar results were found for the DDST language subscale. Another article from the ALSPAC cohort, examined the association between prenatal seafood intake (assessed at 32 weeks gestation) and the child's score on the ALSPAC-adapted DDST communication scale at 6 (N~8750) and 18 months of age (N~8230).[7] Similar to findings from the previous study, children whose mothers consumed 0 grams per week of seafood had higher odds of a low score compared to children whose mothers consumed >340 grams (12 ounces) of seafood per week at both 6 months and 18 months of age.[7] No differences were detected between the >340 grams (12 ounces) per week and 1-340 grams (0-12 ounces) per week consumption groups.[7] The MoBa cohort from Norway (N=38,927) examined the relationship between seafood consumption during the first half of pregnancy (before 22 weeks gestation) and child language and communication impairment at 5 years of age.[23] Three tests were used in this assessment: the ASQ, the Language 20, and the SLAS. Higher seafood intake during pregnancy, when modeled continuously, was associated with less child language and communication impairment across all three tasks; in categorical analyses, benefits tended to only emerge at maternal intake >400 grams (14.1 ounces) per week (compared to 0-100 grams [0 to 3.5 ounces] per week).[23] However, findings were no longer significant after adjusting for maternal mercury exposure among a small proportion of the cohort (N=2232) and gram amounts were difficult to obtain from FFQ data.[23]

The five other articles that utilized assessments specific to language and communication development did not detect statistically significant associations with maternal seafood intake during pregnancy.[8,9,17,22,26] A Chinese cohort study (N=410) did not detect an association between fish intake frequency during pregnancy and child scores on the language domain of the Chinese Pediatric Association-adapted GDS at one year of age.[9] Two PHIME cohort studies (N=606[22] and N=1308)[26] assessed child language development at 18 months of age, finding no association with language scores on the BSID-III.[22,26] A Japanese cohort (N=88) dichotomized maternal seafood intake based on whether the woman was a “frequent” or “less frequent eater”, however, the specific amount of seafood consumed was not assessed and no definition was provided to define frequent and less frequent categories.[28] No associations were found between frequency of maternal seafood intake during pregnancy and scores on any of the three language development scales (receptive language, expressive language, and language concepts) of the KIDS at 18 months of age. Finally, analyses in the Project Viva cohort (N=341) did not detect an association between second trimester seafood intake and child performance on the PPVT at 3 years of age, both in analyses adjusted and unadjusted for maternal erythrocyte mercury and in analyses with different exposure criteria (e.g., fish intake other than shellfish).[17]

Of the eight studies that assessed child language and communication development with verbal IQ and intelligence scales, five detected a beneficial association with seafood intake during pregnancy.[5,7,10,11,13] Consistent with their results utilizing specific scales of language and communication development during infancy and toddlerhood, an article from the ALSPAC cohort (N~5150) detected a beneficial association between higher seafood intake during pregnancy and lower odds of a low score (below 25th percentile) for verbal IQ at 8 years of age, assessed with the WISC-III.[7] Statistically significant differences in odds of receiving a low score on verbal IQ only emerged when comparing children of never consumers to children whose mothers consumed >340 grams (12 ounces) seafood per week, after adjusting for 14 specific nutrients and adjusting for paternal seafood intake separately.[7]
A Spanish INMA study article (N=1590) reported that higher maternal seafood intake during the first trimester was associated with better scores on the verbal subscale of the MSCA at 5 years of age.[10] Specifically, children whose mothers were in the fourth quintile for seafood intake (Median=600 grams [21.2 ounces] per week) scored higher than those in the first quintile (Median=195 grams [6.9 ounces] per week). No statistically significant differences were seen at the highest quintile (Median=854 grams per week) or at the second (Median=338 grams [11.9 ounces] per week) or third (Median=461 grams [16.3 ounces] per week) quintile.[10]

Another Spanish cohort (N=392) that utilized the MSCA detected a beneficial association between fish intake frequency during pregnancy and a detrimental association of shellfish and squid during pregnancy (postnatal assessment) and performance on the verbal subscale at 4 years of age.[13] Specifically, among those who breast-fed less than 6 months, there was a significant association between children whose mothers consumed fish 2-3 times per week, but not 1-2 or >3 times per week, and higher verbal subscale scores compared to children whose mothers consumed fish <1 time per week. Among children breast-fed 6 months or longer, no associations were observed between maternal fish intake and cognitive development, except for an isolated detrimental significant association (with a large confidence interval) between greater fish intake (>3 times per week) compared to < 1 time per week, and lower scores in a memory subscale; no association was seen in children breast-fed for 6 months or longer.[13] In contrast, higher maternal intake of shellfish and squid during pregnancy (>1 time per week vs ≤0.5 times per week) was associated with worse verbal subscale scores.[13] A U.K. cohort reported a significant, beneficial association between seafood intake during late pregnancy (assessed at 32 weeks gestation) and verbal IQ at 9 years of age using the WASI, but not in early pregnancy.[5] When the exposure was oily fish intake only, there was no association between oily fish intake in early or late pregnancy and verbal IQ at 9 years.[5] Finally, a U.S. cohort, (N=107) found that children whose mothers reported consuming any seafood during pregnancy (postnatal assessment I) scored higher on the WPPSI-R verbal IQ scale at 48 months compared to children whose mothers reported no prenatal seafood consumption.[11]

The remaining three studies that assessed child language and communication development with verbal IQ and intelligence scales did not detect associations with maternal seafood intake during pregnancy.[3,4,18] The Mount Sinai Children's Environmental Health Study, (N=162) identified a verbal intelligence factor based on scales from the WPPSI-III and WISC-IV and found no difference in child scores on this factor at 4-9 years of age and maternal report of canned fish intake during pregnancy.[4] Similarly, an Italian cohort, (N=154) found no association between maternal intake of fresh or canned seafood and child verbal IQ at 7 years of age, as assessed by the WISC-III.[3] Finally, consistent with results from the Project Viva cohort at 3 years of age[17], at 6-11 years of age results from this study (N=1068) did not show any associations between maternal seafood intake in mid- or late-pregnancy and child performance on the KBIT-II verbal IQ scale, with and without adjustment for maternal erythrocyte mercury.[18]

Summary

There were notable areas of similarity and dissimilarity in the articles assessing the relationship between seafood intake during pregnancy and aspects of child language and communication development. Four articles were from studies conducted in the U.S. (two from the Project Viva cohort), and two articles each were conducted in the U.K. (both from the ALSPAC cohort), Italy, and Spain; a second PHIME cohort study was conducted in Croatia, Greece, Italy, and Slovenia. Seafood intake during pregnancy was assessed predominantly with FFQs (both validated and those with no information on validation), but the period and timing of the dietary assessment varied greatly, including FFQs administered during each trimester of pregnancy and in the early postpartum period. Furthermore, some studies reported seafood intake in grams per week, others in servings or times per week, and a few in less specific categorizations such as "none vs any" and "frequent vs less frequent eaters". In general, average seafood intake across the cohorts was moderate, with intake tending to be higher in the European cohorts compared to the U.S. cohorts. The type of seafood consumed, which may be an important variable, was not considered in most studies; the one study that considered shellfish and squid separately from fish found divergent results by type. Three studies examined canned seafood, with the type varying by each study: canned fish including tuna, mackerel, and sardines in oil,[3] canned fish (undefined),[4] and canned tuna fish.[17] Aspects of language and communication development were assessed across a wide age range, including children as young as 6 months of age to as old as 11 years of age. Several tests that assessed verbal IQ or intelligence were utilized across multiple cohorts, including the MSCA, the WPPSI (revised and third editions), and the WISC (third and fourth editions). In contrast, scales that assessed language and communication development more specifically were not repeated between cohorts. The potential impact of mercury exposure on the language and communication development outcomes was considered in many studies, but few compared results adjusted and unadjusted for this variable. All but one study[7] were limited by lack of adjustment for at least one key confounder; only half of the articles accounted for most key confounders.[7,9,10,13,18,19,22] Variation in types of seafood assessed, categorization of the seafood exposure (categorically and continuously), tests used to assess outcomes, and child age of test administration, made it difficult to assess precision and compare the magnitude of association between maternal seafood intake and child language and communication indices.

Seafood intake during pregnancy and child movement and physical development

Fourteen articles from nine PCSs examined the relationship between maternal seafood intake during pregnancy and movement and physical development in children.[2,7-13,16-18,22,25,26] Seven articles reported a beneficial relationship between total seafood intake during pregnancy and physical and motor development in children.[7,8,10,11,13,16,17] One article reported a detrimental relationship with asymmetric reflexes in females at 5 weeks of age.[25] The remaining six articles found null associations.[2,9,12,18,22,26] One study found an isolated association between maternal lean fish intake and physical/motor development at 4 years.[10] Results from two cohorts were interpreted with caution due to concerns regarding risk of bias described earlier.[8,11]

In the DNBC (N=25,446), beneficial associations were detected between maternal fish intake during pregnancy, assessed at 25 weeks gestation, and motor development scores of infants at 6 and 18 months of age examined with an investigator developed parent report milestone assessment tool.[16] Specifically, significant associations were found when comparing the first quintile of fish intake (Median=5.9 grams [0.21 ounces] per day) and the highest quintile (Median=50.8 grams [1.8 ounces] per day), but not when comparing it to the intermediate quintiles at 6 months.[16] At 18 months, beneficial associations were detected when comparing the first intake quintile (Median=5.9 grams [0.21 ounces] per day) to the fourth (Median=32.2 grams [1.1 ounces] per day of fish) and fifth intake quintiles (Median=50.7 grams [1.8 ounces] per day).[16]

An article from the Spanish INMA cohort, characterized by high average seafood intake (Median=454 grams [16.0 ounces] per week), assessed the relationship between first trimester seafood intake and child psychomotor development.[10] Maternal seafood intake was assessed using a validated FFQ at approximately 10 to 13 weeks gestation, and child psychomotor development was assessed at 14 months (N=1982) and 5 years of age (N=1589) using the BSID psychomotor scale and the MSCA motor scale, respectively. At 14 months, a beneficial association between first trimester seafood consumption and the BSID psychomotor scale was detected when comparing the second quintile (Median=338 grams [11.9 ounces] per week) to the first quintile (Median=195 grams [6.9 ounces] per week) of seafood intake. No benefit was seen at higher intake levels; total seafood modeled continuously was not associated with psychomotor scale scores.[10] When seafood type was considered, no associations between large fatty fish, small fatty fish, or shellfish intake during the first trimester and child psychomotor scale scores at 14 months were detected.[10] First trimester lean fish intake was associated with child psychomotor scale scores, such that the children born to mothers with third quintile of intake (Median=286 grams [10.1 ounces] per week) performed better than children born to mothers in the lowest quintile of intake (Median=90 grams [3.2 ounces] per week). No other quintiles of lean fish intake were associated with psychomotor scale scores.[10] Performance on the motor subscale of the MSCA at 5 years of age was greater in children born to women in the third (Median=461 grams [16.3 ounces] per week) and fourth (Median=600 grams [21.2 ounces] per week) quintiles of first trimester seafood intake compare to the first quintile of intake (Median=195 grams [6.9 ounces] per week). No associations were seen for the second or highest quintiles of intake.[10]

A New York City cohort examined the association between maternal seafood consumption during pregnancy, assessed with a non-validated questionnaire and dichotomized as none vs any, and child scores on the BSID-II Psychomotor Development Index (PDI) throughout infancy and toddlerhood, adjusted for maternal mercury exposure.[11] Over 70% of the women reported consuming any seafood during pregnancy. Children whose mothers reported consuming any seafood during pregnancy (71.5% of women) had higher BSID-II PDI scores at 36 months of age (N=114), but not at 12 months (N=132) or 24 months of age (N=131).

A Japanese cohort reported a significant beneficial association between seafood intake frequency during pregnancy and higher Kinder Infant Development Scale (KIDS) physical motor subscale and manipulation subscale scores at 18 months based on parental report.[8] Similar to the New York City cohort, this study assessed seafood intake using a non-validated questionnaire and dichotomized maternal seafood consumption as frequent and less frequent eaters.[8] Cut points used to distinguish less frequent and more frequent eaters of seafood were not reported. For both the physical motor and manipulation subscales, children born to more frequent eaters of seafood during pregnancy exhibited better development compared to less frequent eaters.

An article from the ALSPAC cohort in the U.K. examined the association between prenatal seafood intake (assessed at 32 weeks gestation) and child gross motor and fine motor skills, assessed using ALSPAC adapted DDST at 6, 18, 30, and 42 months of age (N~7600-8800).[7] No associations were detected between prenatal seafood consumption and odds of low gross motor or fine motor skills scores (bottom 25th percentile) at 6 and 30 months of age.[7] At 18 and 42 months of age, however, children of mothers who consumed 0 grams per week of seafood, compared to >340 grams (12 ounces) per week of seafood, had significantly higher odds of low fine motor skill scores.[7] No associations were found when comparing intake levels of >340 grams (12.0 ounces) and 1-340 grams (0.0-12.0 ounces) per week and no association between seafood intake during pregnancy and gross motor skills were detected at either 18 or 42 months of age.

A Spanish cohort examined the association of fish and shellfish and squid with child motor skills separately, further stratifying their analyses for fish intake by breastfeeding practices.[13] In this study, a beneficial association between fish intake during pregnancy and motor skills at 4 years assessed using the MSCA was detected in children breastfed for less than 6 months (N=234), specifically when comparing fish intake <1 time per week to >2-3 times per week (but not >3 times per week).[13] No associations were detected between total seafood consumption in women who breastfed > 6 months (N=143) or between maternal intake of shellfish and squid (N=377) and child motor skills at 4 years of age.[13]

Finally, in the Project Viva cohort in the U.S. (N=341), a significant beneficial association between maternal seafood intake during the second trimester and WRAVMA visual-motor subscale scores at 3 years was detected. Specifically, children whose mothers consumed >2 servings per week of seafood had higher scores than children whose mothers did not consume seafood during the second trimester, an association that was similar before and after adjusting for maternal erythrocyte mercury.[17]

Six articles did not detect associations between seafood intake during pregnancy and movement and physical development.[2,9,12,18,22,26] The Seychelles Child Development Study (N=229), a cohort characterized by high maternal fish intake (Mean=537 grams [18.9 ounces] per week, SD=329), examined the relationship between seafood intake during pregnancy and child BSID-II PDI scores at 9 and 30 months of age.[2] Maternal fish intake at 28 weeks gestation (assessed using a food use questionnaire and 4-day food diary) was not associated with child BSID-II PDI scores at 9 and 30 months, before and after adjusting for prenatal methylmercury exposure. Two studies from the PHIME cohort, (N=606[22] and N=1308)[26] found no association between seafood intake during pregnancy and child BSID-III PDI scores at 18 months of age and one on these studies adjusted for total mercury in maternal hair or cord blood.[22] Average total seafood intake varied by the PHIME cohort population and was 2.33 (SD=1.71) servings per week in the Italian subcohort[22] and 1.4 (SD=1.2) servings per week in the full cohort.[26] Unlike results reported previously from the INMA cohort at 14 months[10], a second article from the INMA cohort (N=1683) detected no association between first trimester seafood intake modeled continuously and BSID psychomotor scale scores at 14 months of age in analyses which adjusted for cord blood mercury exposure.[12] A Chinese cohort (N=410) found no association between fish intake during pregnancy, assessed using a dietary assessment method without report of validation, and the child's gross and fine motor development at 1 year of age, using the GDS.[9] Finally, in contrast to the 3 year results reported for the Project Viva cohort, a subsequent article from Project Viva (N=1068) detected no associations between maternal seafood intake during mid- or late-pregnancy and WRAVMA drawing subtest scores at 6-11 years of age.[18]

Finally, a single study (N=344) conducted in the U.S. reported a detrimental association between maternal fish intake during pregnancy and child psychomotor development), in girls (n=182 for females), but not boys, at 5 weeks of age (N=344). When the analysis controlled for maternal or cord blood mercury exposure, the association was no longer significant in girls.[25]

Summary

Inconsistent results were found among studies assessing seafood intake during pregnancy and movement and physical development: seven articles reported beneficial associations[7,8,10,11,13,16,17] whereas six articles found no associations[2,9,12,18,22,26] and one study found an isolated negative association in girls, but not boys, when results were not adjusted for mercury.[25] Most studies used a measure of total seafood or fish intake as their exposure, but two studies assessed the impact of types of fish, such as shellfish and oily fish.[10,13] The timing of the dietary assessments varied from the first trimester to after delivery. Several tests were used to assess psychomotor development, the most common being versions of the BSID among infants and toddlers. All but two studies[7,10] in this body of evidence had a serious risk of bias due to confounding, failing to account or adjust for at least one key confounder. Additionally, four studies used seafood assessments without report of validation,[8,9,11,25] increasing risk for exposure misclassification. The heterogeneity of these studies makes it difficult to determine a conclusion regarding the relationship between maternal seafood intake during pregnancy and movement/physical development.

Seafood intake during pregnancy and social-emotional and behavioral development

Nine articles examined the relationship between seafood and fish intake during pregnancy and social-emotional and behavioral development in the child. Six articles from four PCSs examined outcomes among children ages 6 months through 42 months[1,7-9,22,25] and 4 articles from three PCSs examined outcomes among children between ages 4 years and 13 years.[4,5,7,14]

Three articles from the ALSPAC cohort in the U.K. examined the relationship between seafood intake during pregnancy (assessed at 32 weeks gestation) and child social-emotional and behavioral development across childhood.[1,7,14] One study in China examined the relationship between fish intake during pregnancy and the adaptive domain using the GDS at 1 year of age.[9] The HOME study in the U.S. examined maternal fish intake during pregnancy and need for special handling using the NNNS at 5 weeks of age.[25]

An article from the ALSPAC cohort examined maternal seafood intake during pregnancy (mean=235 grams [8.3 ounces] per week) using a validated FFQ at 32 weeks gestation.[7] Social-emotional development was assessed using the ALSPAC-adapted DDST at 6, 18, 30, and 42 months (N~7600-8750) and the SDQ total score, and prosocial, emotional, conduct, and peer problems subscales at 7 years of age (N~6580). A significant association between maternal seafood intake during pregnancy and lower odds of being in the bottom quartile for DDST measured social development at 30 and 42 months of age, but not at 6 or 18 months of age, was detected. Specifically, the study reported that seafood intake of 0 grams per week, compared to >340 grams (12 ounces) per week, was associated with 24% greater odds of being in the bottom quartile for social development at 30 months.[7] No associations were found when comparing >340 grams (12 ounces) per week to 1 to 340 grams (0 to 12 ounces) per week of seafood. Among children aged 42 months, seafood intake of 1 to 340 grams (0 to 12 ounces) per week during pregnancy, compared to >340 grams (12 ounces) per week, was associated with 17% greater odds of being in the bottom quartile for social development.[7] No associations with social development were found when a seafood intake level of 0 grams per week was compared to >340 grams (12 ounces) per week. Utilizing the SDQ, one statistically significant association was detected out of six scales or subscales.[7] Specifically, maternal consumption of 0 grams per week of seafood, compared to consuming >340 grams (12 ounces) per week, was associated with a 44% greater odds of low scores (bottom ~10th percentile) on the prosocial subscale at 7 years of age.[7] There were no significant associations between maternal seafood intake during pregnancy and the SDQ total score or the hyperactivity, emotional, conduct, and peer problems subscales at 7 years.[7]

A second article from the ALSPAC study examined the relationship between seafood intake during pregnancy and child social-emotional development in the ALSPAC cohort (N=7421), utilizing the ALSPAC adaption of the DDST and the MCDI.[1] Approximately 39% of the study population reported consuming fish 4 or more times per week during pregnancy, with 42% consuming white fish 1 to 3 times per week and 25% consuming oily fish 1 to 3 times per week.[1] A significant trend between increasing prenatal fish intake and higher MCDI social activity scores at 15 months of age was detected.[1] Consistent with this trend, children whose mothers consumed fish during pregnancy 1-3 meals per week and 4 or more meals per week, compared to children whose mothers "rarely or never" consumed fish, had lower odds of scoring in the lowest 15th percentile for the MCDI social activity scale. Maternal fish consumption at all levels above "rarely or never" was associated with greater odds of scoring in the highest 15th percentile.[1] As was seen in the ALSPAC cohort, no association between maternal fish intake and child social development at 18 months of age as measured by the DDST was detected.[1] When analyses were adjusted for cord mercury levels, in a small subset with this data available (N=1054), similar results for both the MCDI and DDST were observed, however these data were not reported.

A third article from the ALSPAC cohort addressed social-emotional development, analyzing a subset of the full cohort which was restricted to individuals with either early-onset conduct problem (EOP) or low conduct problem (low CP) trajectories throughout childhood as identified by the SDQ (N=5493).[14] Mothers whose children were identified as having an EOP trajectory had a mean fish intake of ~1.83 servings per week, which was significantly lower than that of mothers whose children were identified as having a low CP trajectory (Mean~2.07 servings per week).[14] Additionally, the study assessed the association between fish intake and the emotional difficulties and hyperactivity subscales of the SDQ, examined at 4-10 and 12-13 years of age.[14] No association between maternal fish intake and either subscale was detected when the children were 4-10 years of age. When assessed at 12-13 years of age, however, maternal seafood intake of ≥2 servings per week during pregnancy was associated with fewer emotional difficulties in children compared to <2 servings per week in the EOP trajectory group; no association between maternal fish intake and emotional difficulties was detected in the CP trajectory group.[14] The risk of bias due to selection of participants was serious in this particular study, in that they selected children with the highest and lowest conduct problems, omitting those with intermediate conduct problem trajectories.[14]

Another study examined total fish consumption during pregnancy and its relationship to child GDS adaptive and social domain scores at 1 year in a Chinese sample (N=410) with approximately one third of mothers reporting fish consumption of at least 1 time per week.[9] There was a statistically significant association between increasing prenatal fish intake categories and better infant adaptive domain scores; however, no association between maternal fish intake during pregnancy and infant social domain scores was detected.[9] Finally, a U.S. cohort (N=270), examined the relationship between total fish consumption during pregnancy (Median=13 fish-containing meals across pregnancy, interquartile range: 6-17) and infant need for special handling at 5 weeks of age.[25] When modeling fish intake during pregnancy continuously, greater fish intake was associated with less need for special handling at 5 weeks of age, with and without adjustment for maternal mercury exposure.[25] However, the findings were no longer significant after adjusting for cord total mercury instead of maternal total mercury.[25]

The remaining four studies did not detect an association between maternal seafood consumption during pregnancy and social-emotional and behavioral development at 18 months,[8,22] at 4-9 years,[4] and at 9 years of age.[5] Two PHIME cohort studies, assessed maternal fish consumption during pregnancy, continuously (N=606)[22] and (N=1308)[22], and reported no association with social-emotional and adaptive behavior subscale scores of the BSID-III at 18 months.[22,26] One of these studies reported a mean intake of 2.33 servings of fish, mollusk, and crustaceans per week, most of which can be attributed to fresh, frozen, or canned fish (Mean=1.69 servings per week).[22] A Japanese cohort study assessed the association between maternal seafood intake during pregnancy and a variety of social and behavioral subscales using the KIDS at 18 months.[8] No significant associations were detected between seafood intake during pregnancy, comparing frequent vs less frequent eaters with an undefined cutoff, and child subscale scores for social relationships with children and with adults, discipline (self-caring behaviors), and feeding (eating and drinking behaviors).[8]

A U.S. cohort study did not find an association between maternal canned fish consumption during pregnancy (N=162, <1 time per week versus ≥ 1 time per week) and factor scores for impulsivity and externalizing, executive functioning, internalizing, and adaptability, derived from assessments using the BRIEF and BASC at 4-9 years.[4] The majority (~87%) of mothers in this sample reported consuming canned fish less than 1 time per week.[4] Finally, a U.K. cohort (N=217) examined the relationship between maternal seafood intake in early (FFQ completed at 15 weeks gestation) and late pregnancy (FFQ completed at 32 weeks gestation) and child maladaptive behaviors at 9 years of age with the SDQ.[5] In this sample, approximately two thirds of the cohort reported consuming fish at least 1-2 times per week during early pregnancy and late pregnancy.[5] There were no significant associations between total seafood intake at either early or late pregnancy and the SDQ total difficulties score, or any subscale including hyperactivity, conduct problems, peer problems, or emotional symptoms. When maternal oily fish intake was considered, an isolated benefit was detected for the hyperactivity subscale, with higher intakes in early and late pregnancy, but no other subscale or the SDQ total difficulties score varied by maternal oily fish intake.

Summary

There are several limitations common across the body of evidence. Only one of the articles[7] accounted for all of the key confounders. Only two articles considered the potential impact of maternal mercury exposure on the reported associations between maternal seafood intake during pregnancy and social-emotional and behavioral development,[1,22] whereas six articles did not.[4,5,7-9,14] There were also limitations in the measurement of the exposure, including non-validated questionnaires,[8,9] unknown times of seafood intake assessments,[8] unknown cut points used to determine exposure groups,[8] and assessments of limited types of fish such as only canned fish intake.[4] The timing of seafood intake varied across studies: seafood exposures were assessed during all trimesters of pregnancy, but only one study assessed seafood and fish intake at multiple time points in pregnancy.[5] Most social-emotional and behavioral outcomes relied on parental-report measures, including the ALSPAC-adapted DDST and MCDI, SDQ, BASC, BRIEF, and KIDS.

Seafood intake during pregnancy and ADD/ADHD

No studies meeting inclusion criteria examined the relationship between seafood consumption during pregnancy and diagnosis of ADD or ADHD. Four articles from three prospective cohorts examined the association between maternal seafood intake during pregnancy and ADD/ADHD-like traits or behaviors: two articles from the ALSPAC cohort in the U.K.,[7,14] one article from another cohort in the U.K.,[5] and one article from the New Bedford Cohort in the U.S.[20] The study characteristics of these four articles can be found in **Table 1**, and the results can be found in **Table 3**. Of these four articles, two detected protective associations between maternal seafood intake and ADD/ADHD-like behaviors and traits[5,20] whereas two found no such association.[7,14]

Two studies found significant associations between seafood intake during pregnancy on ADD/ADHD-like traits.[5,20] A U.K. cohort assessed the relationship between total maternal seafood intake during pregnancy and oily fish intake during early and late pregnancy separately (N=217) and hyperactivity using the SDQ.[5] Few women in this cohort never consumed seafood (9%) with most consuming <1 or 1-2 times per week. A higher proportion of women reported never consuming oily fish during early pregnancy (29%) or late pregnancy (32%) compared to seafood (9%). Maternal total seafood intakes during early pregnancy (assessed at 15 weeks gestation) or late pregnancy (assessed at 32 weeks gestation) were not associated with odds of high scores on the hyperactivity subscale at 9 years of age, with a higher score indicating greater hyperactivity.[5] However, a significant association between oily fish consumption in both early and late pregnancy and lower odds of having a high hyperactivity subscale score was detected, particularly when comparing children of never consumers to those who consumed oily fish <1 time per week. No analyses from this study accounted for maternal mercury exposure.

A U.S. cohort (N~508) examined the relationship between maternal total seafood intake during pregnancy (reported shortly after birth) and ADHD-like traits and behaviors among children aged 8 years using the CRS-T.[20] The mean maternal seafood intake during pregnancy in this cohort was 3.7 servings per week (SD=3.9). In this study, consuming >2 serving per week of total seafood, compared to ≤ 2 servings per week, was significantly associated with lower risk of receiving mild or markedly atypical scores on the inattentive subtype, impulsive/hyperactive subtype, and total (subtypes combined) subscale scores. Results were similar between analyses adjusted and unadjusted for maternal total hair mercury.

In summary, a U.K. study did not find a significant association between total seafood consumption during pregnancy and hyperactivity symptoms, but did find an association between oily fish intake and SDQ hyperactivity subscale scores at 9 years of age.[5] A U.S. study found a significant association between seafood consumption during pregnancy and lower odds of inattentiveness and impulsive/hyperactivity CRS-T subscale scores at 8 years of age.[20]

Two articles from the ALSPAC cohort did not detect any significant associations between seafood intake during pregnancy and hyperactivity symptoms as assessed by the SDQ at either 7 years of age (N~6580)[7] or between the ages of 4-10 years and 12-13 years (N=5493).[14] Articles from the ALSPAC cohort measured total maternal seafood intake during pregnancy at 32 weeks gestation, and the reported mean intake in one article was 235 grams per week (SD=202)[7] and ~2 servings per week in the other.[14] Neither article accounted for maternal mercury in their analyses.

Summary

There were similarities among the four articles that evaluated maternal seafood intake during pregnancy and ADD/ADHD-like traits and behaviors. Three articles were from studies conducted in the U.K. (two from the ALSPAC cohort) and one article was from a study conducted in the U.S. All studies assessed total seafood intake during pregnancy using a FFQ; three studies assessed intake at 32 weeks, and average seafood intake levels were moderate. In all four studies, results were analyzed categorically, either based on number of servings with 2 servings per week as a cut point[5,14,20] or with an intake of 340 grams or 12 ounces per week as a cut-point.[7] All studies assessed school-aged children between 4 to 13 years of age, with three of four studies using parental report of SDQ scales to assess hyperactivity behaviors and traits. No association was found in the studies from the ALSPAC cohort, which used a validated FFQ. One study found a protective association between maternal oily fish intake and hyperactivity scores at 9 years of age. No studies assessed the association between maternal seafood intake during pregnancy and diagnoses of ADD/ADHD. Only one study considered the potential impact of maternal mercury exposure; it reported minimal impact on the relationship between maternal seafood intake during pregnancy and child ADD/ADHD-like traits and behaviors.[20]All but one study[7] were limited by the lack of adjustment for key confounding variables Due to the limited number of studies and the inconsistency in results, a conclusion about the relationship between maternal seafood intake during pregnancy and ADD/ADHD-like traits or symptoms is difficult to determine.

Seafood intake during pregnancy and ASD

Three articles from PCSs examining maternal seafood intake during pregnancy and ASD-like behaviors or traits in offspring were included in this review. One article was from the ALSPAC cohort in the U.K.,[6] one article was from the INMA cohort in Spain,[10] and one article was from the Generation R cohort in the Netherlands.[21] The characteristics of these three studies are found in **Table 1** and the results are found in **Table 3**. Two studies examined total seafood intake during pregnancy and ASD-like behaviors,[10,21] whereas one study examined shellfish, white fish, and oily fish exposures in relation to both ASD-like behavior and autism diagnosis.[6] One study also examined types of fish including large fatty fish, lean fatty fish, oily fish, small fatty fish, and white fish, and the relationship to ASD-like traits or behaviors.[10] Two studies examined whether shellfish intake was related to ASD-like behaviors.[6,10]

One article from the well-designed INMA cohort (N=1393) assessed the association between maternal total seafood consumption and ASD-like traits.[10] This study found that higher total seafood intake during the first trimester was associated with reduced ASD-like traits (assessed via the CAST) in children at 5 years of age. This was observed when seafood intake was modeled continuously and when comparing the first quintile of intake (Median=195 grams [6.9 ounces] per week) to the fourth quintile

(Median=600 grams [21.2 ounces] per week) or fifth quintile (Median=854 grams [30.1 ounces] per week) of intake.[10] There were no statistically significant differences at the lowest quintiles (median=195 grams [6.9 ounces] per week compared to median=228 grams [8.0 ounces] or 461 grams [16.3 ounces] per week), suggesting that high seafood intake during pregnancy may be needed to observe a relationship between seafood and ASD-like traits.[10] However, in another analysis which included all individuals with ≤340 grams (12 ounces) per week of seafood as the reference group (N=446), no significant associations between maternal seafood consumption and ASD-like traits were found.[10] Baseline average maternal seafood intake during early pregnancy, assessed at 10-13 weeks gestation, in this Spanish population was 498 grams (17.6 ounces) per week (median=454 grams [16.0 ounces] per week), higher than current 2015-2020 Dietary Guidelines for Americans recommendation for 227 grams (8.0 ounces) to 340 grams (12.0 ounces) per week.[ii] Regarding different types of fish, the study detected a positive association between both large fatty fish intake (modeled categorically and continuously) and lean fish intake (only when modeled categorically), and reduced ASD-like traits at 5 years of age; no association between small fatty fish intake and ASD-like traits was detected.[10] Regarding shellfish, maternal shellfish consumption during the first trimester was significantly associated with reduced ASD-like traits (assessed via the CAST) when comparing the first quintile of intake (Median=0 grams per week) and the third quintile of intake (Median=49 grams [1.7 ounces] per week).[10] However, no significant differences were found between the first quintile and any other quintile of shellfish intake, nor was an association detected when analyzed continuously.[10]

Two of three articles did not detect an association between fish intake during pregnancy and ASD-like traits at 6 years[21] and at 3, 5, 7, and 9 years.[6] In the Generation R cohort from the Netherlands, which examined total seafood intake in early pregnancy (N=3802), no association between maternal fish intake and child ASD-like traits (assessed via the SRS) at 6 years of age was detected.[21] Average fish intake in this cohort was relatively low, averaging 11.5 grams [0.4 ounces] per day (range: 1.4-50.5 grams [0.05 to 1.8 ounces] per day) and was assessed at 14 weeks gestation.[21] In an article from the ALSPAC cohort in the U.K., there were no associations between either oily fish intake or white fish intake and ASD outcomes.[6] Fish intake was assessed at 32 weeks gestation and child ASD-like traits (i.e., poor sociability, repetitive behavior, poor social cognition, poor coherence) were assessed between 3 and 9 years of age (N~8000) and ASD diagnosis by 11 years of age (N~1200).[6] Average fish intake in this cohort was not reported.[6]

Summary

Three European PCSs assessed the association between maternal seafood intake and child ASD-like traits or behaviors in children 3 to 9 years of age,[6,10,21] with one also assessing ASD diagnosis by 11 years.[6] One of three studies found a significant, protective association between maternal seafood intake and ASD-like traits in children.[10] Specifically, in a population with high seafood intake (~498 grams [17.6 ounces] per week), this study found a protective association between some intake

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[ii] U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015-2020 Dietary Guidelines for Americans. 8th Edition. December 2015. Available at http://health.gov/dietaryguidelines/2015/guidelines/.

levels of total seafood, fatty fish, and to a lesser degree lean fish intake and ASD-like traits. In contrast, two other studies found no association between maternal seafood intake and ASD-like traits or ASD diagnosis.[6,21] The three European studies relied on questionnaires based on parental report to assess ASD-like traits and behaviors, whereas diagnosis of ASD was assessed through a variety of methods including educational records and parental report. No study considered the potential impact that maternal mercury exposure may have had on the reported associations between seafood intake during pregnancy and child ASD-like traits or ASD diagnosis. The three studies failed to account or adjust for at least one key confounder, one of which did not control for many key confounders.[6] Due to the limited number of studies, limitations in methodology, and the inconsistency in results, a conclusion about the relationship between maternal seafood intake during pregnancy and ASD-like traits and behaviors or ASD diagnosis was difficult to determine.

Assessment of the evidence[iii]

As outlined and described below, the body of evidence examining seafood consumption during pregnancy and lactation and neurocognitive development in the child was assessed for the following elements used when grading the strength of evidence.

- **Risk of bias (Table 4):** There were some concerns that systematic errors resulting from the design and conduct of the studies could have influenced the reported results across the body of evidence. Risk of bias trends were fairly consistent across outcomes and was primarily attributed to:
    - Risk of bias due to confounding: Only one article accounted for all key confounders identified *a priori* in the systematic review protocol[10]; however, eleven articles accounted for most of the key confounders.[7-10,12,13,16-18,21,22] Non-fish dietary exposure to n-3 PUFA, race/ethnicity and maternal anthropometrics were not commonly adjusted for in analyses.
    - Risk of bias in selection of participants into the study: One study had a serious risk of selection bias because participants with high and low scores on the SDQ were selected into the study and those with intermediate scores were excluded.[14]
    - Risk of bias due to classification of exposures: Some studies did not provide validation for or used poorly described FFQs, questionnaires, or surveys to assess maternal seafood intake during pregnancy. The measurement error inherent in all self-reported dietary data was an unavoidable limitation.
    - Risk of bias in selection of the reported result: One study had a serious risk of bias in selection of the reported result because there was no report

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[iii] A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

of the relationship between seafood intake during the third trimester and some neurocognitive outcomes based on the BSID and CAST.[10]

- **Consistency:** Results were predominantly beneficial or null, with few detrimental results. The most consistent results were observed for cognitive development. Inconsistency is likely due to heterogeneity in the types and amounts of seafood intake, the methods used to categorize and analyze seafood intake, ages of children at follow-up, and the neurocognitive assessment measures.
- **Directness:** The large majority of studies were designed to examine maternal seafood intake and neurocognitive outcomes. However, some studies were designed primarily to examine environmental contaminants.[2,8,9,11,12,25] Among studies evaluating ADD/ADHD, no study included a clinical or comprehensive psychological evaluation and among studies evaluating ASD, only one considered a clinical diagnosis.[5]
- **Precision:** Evidence from 26 articles, from 18 PCSs, was evaluated. Few studies reported *a priori* power analyses and it is likely that several studies and sub-analyses were underpowered. Large variations in assessment types, scales or indices, and age at assessment made evaluation of precision and comparison of magnitude of associations across studies difficult.
- **Generalizability:** Six articles from U.S. studies, most conducted in the northeast, consisted of ethnically and racially diverse participants. Socioeconomic status and education level were moderate to high in the majority of studies. Numerous studies were conducted in northern or southern Europe, where the average seafood intake is generally higher than in the U.S.

Other considerations

- A large, comprehensive search was conducted in multiple databases for this systematic review. Although risk of publication bias is always of potential concern, both small and large studies were included in this review, reporting both null and statistically significant results. Therefore, risk of publication bias is likely low across this body of evidence.

Research recommendations

In order to better assess the relationship between maternal seafood consumption during pregnancy and/or lactation and child neurocognitive outcomes, additional research is warranted. Should research in this area be conducted, the following recommendations should be considered to improve comparability across studies:

- Seafood intervention/exposure:
    - Validated and reliable methods to assess the amount, frequency, type, source, and preparation of seafood consumed by women at multiple, defined time points during pregnancy and lactation.
    - Consistency in defining seafood intake categories to compare seafood intake levels across studies
- Increased use of validated and reliable outcome assessment methods particularly for language and behavioral outcomes, and use of standardized outcome assessment methods.

- Increased use of more objective outcome assessment tools that do not rely on parental-report, particularly for social-emotional and behavioral outcomes.
- More consistent accounting or adjustment for maternal methyl mercury exposure is needed to better understand the potential associations between seafood intake during pregnancy and/or lactation and child neurocognitive outcomes.
- More consistent accounting or adjustment for key factors that could impact the relationship between maternal seafood intake during pregnancy and lactation and child neurocognitive outcomes (e.g., non-fish dietary exposure to n-3 PUFAs).
- Increased research is needed in diverse populations.
- More research is needed in the following topic areas:
    - Maternal seafood intake during lactation and child neurocognitive outcomes
    - Maternal seafood intake during pregnancy and/or lactation and diagnosis of ADD/ADHD and ASD, in addition to ADD/ADHD-like and ASD-like traits and behaviors.
    - Maternal seafood intake during pregnancy and/or lactation and academic performance, anxiety, and depression.

Included articles

1. Barbone F, Rosolen V, Mariuz M, et al. Prenatal mercury exposure and child neurodevelopment outcomes at 18 months: Results from the Mediterranean PHIME cohort. *Int J Hyg Environ Health*. 2019;222(1):9-21. doi:10.1016/j.ijheh.2018.07.011.
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Table 1. Study characteristics of studies that examined the relationship between seafood consumption during pregnancy and neurocognitive development in the child[iv,v]

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations
Avon Longitudinal Study of Parents and Children (ALSPAC) Cohort Studies		

Daniels, 2004[1]
Prospective Cohort Study, ALSPAC, U.K.
Baseline N=10,092 Analytic N=7,421 (Attrition: 26%)
 	
Participant characteristics:
• Maternal age: Mean=29y, SD=5
• Female child: 48%
• Race/Ethnicity: NR
• SES: Mother's educational level: very low 10%, low 9%, moderate 36%, moderately high 26%, high 15%
• Parity: 45% primiparous
• Pre-pregnancy BMI/wt at conception: NR
• GWG: NR
 	
Maternal seafood exposure during pregnancy:
• Fish intake: Rarely/never 12%, <1/wk 18%, 1-3/wk 31%, 4+/wk 39%
• White fish intake: Rarely/never 16%, <1/wk 40%, 1-3/wk 42%, 4+/wk 2%
• Oily fish intake: Rarely/never 38%, <1/wk 34%, 1-3/wk 25%, 4+/wk 1%
 	
Seafood nutrient exposure: NR
 	
Mercury exposure:
• Total cord mercury (N=1054), Geometric mean (SD): 0.01 µg/g (0.4)
 	
Infant feeding practices:
• Child ever breastfed: 67%
• Child ate fish 1+/wk at 6mo: 44%
• Child ate fish 1+/wk at 12mo: 81%
	Exposure:
	Maternal fish intake (meals/wk) during pregnancy assessed at 32wk gestation
	
	Assessment method:
	Fish intake (including white fish [cod, haddock, plaice, fish fingers, etc.], oily fish (pilchards, sardines, mackerel, tuna, herring, kippers, trout, salmon, etc.)) assessed via partially validated FFQ
	
	Outcomes and assessment methods:
	Childhood development
	• ALSPAC-adapted DDST (Denver Developmental Screening Test) at 18mo (parental report):
	  ○ Total score (aggregates scores for language, social, fine and gross motor skills)
	  ○ Language subscale
	  ○ Social subscale
	Language and communication development
	• ALSPAC-adapted MCDI (MacArthur Communicative Development Inventory) at 15mo (parental report):
	  ○ Vocabulary comprehension subscale
	  ○ Social activity subscale
		Confounders accounted for:
		Child sex, child age, parity, maternal age, parental education, SES, smoking, alcohol intake, fish intake at other times, breastfeeding status, dental treatment, HOME score
		
		Limitations:
		• Several key confounders not accounted for: child birthweight, gestational age, race/ethnicity, maternal anthropometrics, non-fish dietary exposure to n-3 PUFA
		• Maternal mercury accounted for only small subset of participants
		• ALSPAC-adapted DDST and MCDI rely on parental report

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Golding, 2018[6]
Prospective Cohort Study, ALSPAC, U.K.
Baseline N=14,062 Analytic N=8,000 (Attrition: 43%)
 	
Participant characteristics:
• Maternal age: NR
• Female child: NR
• Race/Ethnicity: NR
• SES: NR
• Parity: NR
• Pre-pregnancy BMI/wt at conception: NR
• GWG: NR
 	
Maternal seafood exposure: NR
 	
Seafood nutrient exposure: NR
 	
Mercury exposure:
• Prenatal maternal blood mercury by fish exposure, Mean (SD):
• White Fish Frequency: Not at all 1.63 µg/L (1.02); Once in two wk, 2.09 µg/L (0.99); >Once a wk, 2.35 µg/L (1.14); P<0·0001
• Oily Fish Frequency: Not at all, 1.75 µg/L (0.94); Once in two wk, 2.28 µg/L (1.08); >Once a wk 2.50 µg/L (1.19)
• Shell Fish Frequency: Not at all, 2.02 µg/L (1.05); Any, 2.49 µg/L (1.19)
 	
Infant feeding practices: NR
	Exposure:
	Maternal intake of white fish, oily fish, and shell fish assessed at 32wk gestation
	
	Assessment method:
	Three validated FFQ questions measuring frequency with which the mother ate white fish, oily fish, and shellfish (partially validated by comparing responses with levels of DHA measured in maternal prenatal red blood cells)
	
	Outcomes and assessment methods:
	Child autistic traits (parental report)
	• EAS (Emotionality, Activity, Sociability temperament traits/scale):
	  ○ Sociability at 3y
	• ALSPAC derived measure of repetitive behavior at 5y
	• SCDC (Social and Communication Disorders Checklist):
	  ○ Social communication at 7y
	• CCCCS (Child Communication Checklist Coherence Scale):
	  ○ Coherent speech at 9y
	
	Autism diagnosis by 11y
	• Identified by either educational records, maternal/parental report, classification as "Pervasive Development Disorder" from DAWBA questionnaire
		Confounders accounted for:
		Child age, maternal age, parental education, SES, housing tenure
		Autism traits, not autism diagnosis: parity, smoking, alcohol intake, family adversity index, household crowding, life events, breastfeeding
		Autism diagnosis only: time lived in Avon, and maternal locus of control
		
		Limitations:
		• Several key confounders not accounted for: child birthweight, gestational age, race/ethnicity, maternal anthropometrics, SES, non-fish dietary exposure to n-3 PUFA; family history of autism
		• Did not account for maternal mercury exposure
		• No information provide describing subject selection nor analysis to address missing data
		• Number of autism cases was low, limiting statistical power
		• Identification of autism cases used a multi-source ascertainment approach and misclassification could have occurred
		• EAS, SCDC, CCCCS, and ALSPAC derived measure of repetitive behavior rely on parental report
		• Baseline characteristics data not reported

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations
Hibbeln, 2007[7] **Prospective Cohort Study, ALSPAC, U.K.** Baseline N=8,946 Analytic N=5,449 (Attrition: 39%) **Participant characteristics:** • Maternal age: <20y, ~2%; ≥20y, ~98% • Female child: ~48% • Race/Ethnicity: White: ~98.8%, Black: ~0.7%, Asian: ~0.5% • SES: Maternal education: Low, ~25%; Middle, ~36%; High, ~39%; Housing: Mortgaged/owned, ~81%; Council, ~10%; Other, ~9%; Crowding at home: <1 person/room, ~85%; 1+person/room, ~15%; Partner: Yes, ~98%; No, ~2% • Parity: 0, ~44%; 1, ~36%; 2+, ~20% • Pre-pregnancy BMI/wt at conception: NR • GWG: NR **Maternal seafood exposure:** • Seafood intake, Mean (SD): 235 g/wk (202), range: 0-3268 g/wk • Seafood intake: None, 12%; 1-340 g/wk, 65%; >340 g/wk, 23% **Seafood nutrient exposure:** • Maternal n-3 fatty acids from seafood, Mean (SD): 1.06 g/wk, (1.05), range: 0-15.6 g/wk **Mercury exposure:** NR **Infant feeding practices:** Breastfed: ~80%	**Exposure:** Maternal seafood intake (g/wk) during pregnancy assessed at 32wk gestation **Assessment method:** Seafood intake (including white fish, dark or oily fish, shellfish) via self-reported FFQ, validated in relation to two biochemical markers in the ALSPAC subpopulation **Outcomes and assessment methods:** Child development • ALSPAC-adapted DDST (Denver Developmental Screening Test) at 6mo, 18mo, 30mo, 42mo (parental report): o Gross motor o Fine motor o Social development o Communication Childhood behavior • SDQ (Strengths and Difficulties Questionnaire) at 7y (parental report): o Total score o Prosocial subscale o Hyperactivity subscale o Emotional subscale o Conduct subscale o Peer problems subscale Cognition • WISC-III (Wechsler Intelligence Scale for Children III) at 8y: o Full scale IQ o Verbal IQ o Performance IQ	**Confounders accounted for:** Child sex, child age, child birthweight, gestational age, parity, race/ethnicity, maternal age, maternal anthropometrics, parental education, SES, smoking, alcohol intake, non-fish dietary exposure to n-3 PUFA, housing, crowding at home, life events, partner, breastfeeding **Limitations:** • One key confounders not accounted for: non-fish n-3 PUFA exposure • Did not account for maternal mercury exposure • ALSPAC-adapted DDST and SDQ rely on parental report

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Mesirow, 2017[14]
Prospective Cohort Study, ALSPAC, U.K.
Baseline N=13,988 Analytic N=5,493 (Attrition: 61%)
 	
Participant characteristics:
• Maternal age: NR
• Female child: 50.1%
• Race/Ethnicity: Caucasian/White ~98%
• SES: Social class, Low SES ~9%, Inadequate housing ~12%, Lack of basic living conditions ~7%, Housing defects/infestations ~27%, No educational qualifications (mother or partner) ~10%, Financial difficulties ~19%
• Parity: ~36% primiparous
• Pre-pregnancy BMI/wt at conception: NR
• GWG: NR
 	
Maternal seafood exposure during pregnancy:
• Fish intake during pregnancy (Mean): ~2 svg/wk
 	
Seafood nutrient exposure: NR
 	
Mercury exposure: NR
 	
Infant feeding practices: Never breastfed (first 6mo): ~16%
	Exposure:
	Maternal fish intake during pregnancy assessed at 32wk gestation
	
	Assessment method:
	Fish intake (including white fish, oily fish, and shellfish) measured via partially validated FFQ
	
	Outcomes and assessment methods:
	Child emotional difficulties and hyperactivity
	• SDQ (Strengths and Difficulties Questionnaire) at 4-13y (parental report):
	  ○ Emotional difficulties subscale
	  ○ Hyperactivity subscale
		Confounders accounted for:
		Child sex, child age, parental education, SES, alcohol intake, total energy intake (prenatal)
		
		Limitations:
		• Several key confounders not accounted for: child birth weight, gestational age, parity, race/ethnicity, maternal age, maternal anthropometrics, smoking, non-fish dietary exposure to n-3
		• Did not account for maternal mercury exposure
		• SDQ relies on parental report
		• Serious risk of selection bias: participants selected based on high or low scores on the SDQ, those with intermediate scores excluded

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Williams, 2001[24]
Prospective Cohort Study, ALSPAC, U.K.
Baseline N=641 (randomly selected subset of children born in last 6mo of cohort enrollment; Cohort N~12,000) Analytic N=435 (Attrition: 32%)
 	
Participant characteristics:
• Maternal age: <25y 15.6%, 25-29y 40.5%, ≥30y 43.9%
• Female child: 47.9%
• Race/Ethnicity: NR
• SES: Maternal education: Secondary 12.4%, Vocational 9.6%, O level 32.2%, A level 27.3%, Degree 18.5%; Financial difficulties: None 34.9%, Some 38.7%, Many 25.7%
• Parity: 49.9% primiparous
• Pre-pregnancy BMI/wt at conception: NR
• GWG: NR
 	
Maternal seafood exposure during pregnancy:
• Any fish intake: Yes 77.2%, No 22.8%
• White fish intake: Yes 82.6%, No 17.4%
• Oily fish intake: Yes 61.2%, No 38.8%
• Shellfish intake: Yes 24.4%, No 75.6%
 	
Seafood nutrient exposure:
• Maternal erythrocyte DHA concentrations in pregnancy, Mean: 2.71%
 	
Mercury exposure: NR
 	
Infant feeding practices:
• Breastfed:
  ◦ Never 24.9%
  ◦ Stopped by 4mo 31.2%
  ◦ Still at 4mo 43.9%
• Child eats oily fish at 36mo: Yes 44.0%, No 56.0%
	Exposure:
	Maternal intake of white fish, oily fish, and shellfish during pregnancy, assessed at 32wk gestation
	
	Assessment method:
	Seafood intake (including white fish (cod, haddock, plaice, and fish fingers) and oily fish (pilchards, sardines, mackerel, tuna, herring, kippers, trout, and salmon)) measured via partially validated FFQ
	
	Outcomes and assessment methods:
	Stereoacuity
	• Orthoptist administered book-format random dot stereoacuity test at 3.5y
		Confounders accounted for:
		Child sex, child age, parity, maternal age, parental, SES, smoking, breastfeeding, child has paid child care, mother has had paid job since child's birth, mother is a vegetarian, mother eats any fish, mother eats white fish, mother eats shellfish, mother eats oily fish, child eats oily fish
		
		Limitations:
		• Several key confounders not accounted for: child birthweight, gestational age, race/ethnicity, maternal anthropometrics, alcohol intake, non-fish dietary exposure to n-3 PUFA
		• Did not account for maternal mercury exposure
		  ◦ Stereopsis testing at 3.5y is difficult and repeatability of test was only moderately reliable (intraclass correlation
		  ◦ coefficient=0.39)

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Davidson, 2008[2]
Prospective Cohort Study, Seychelles Child Development Study, Seychelles Baseline N=283 Analytic N=229 (Attrition: 19%)
 	
Participant characteristics:
• Maternal age: Range: 16-43y
• Female child: ~51%
• Race/Ethnicity: NR
• SES: NR
• Parity: NR
• Pre-pregnancy BMI/wt at conception: NR
• GWG: NR
 	
Maternal seafood exposure:
• Fish intake at 28wk gestation (Mean): 76.7 g/d (537 g/wk, ~9 meals/wk), SD=47.0 (range: 0-346.3 g/d)
• Most frequently consumed fish species in Seychelles: Karang, Shoemaker, Tuna, Mackerel, Barracuda
 	
Seafood nutrient exposure:
• Maternal blood DHA at 28wk gestation, Mean (SD): 0.19 mg/ml, (0.06), range: 0.07-0.4 mg/ml
• Maternal blood DHA at delivery, Mean (SD): 0.16 mg/ml (0.06), range: 0.06-0.3 mg/ml
• Maternal blood AA at 28wk gestation, Mean (SD): 0.63 mg/ml, (0.14), range: 0.4-1.2 mg/ml
• Maternal blood AA at delivery, Mean (SD): 0.60 mg/ml (0.15), range: 0.3-1.2 mg/ml
 	
Mercury exposure:
• Maternal hair mercury, Mean (SD): 5.7 ppm (3.7), range: 0.2-18.5 ppm
 	
Infant feeding practices: NR
	Exposure:
	Maternal fish intake (g/d) during 26-28wk gestation assessed at 28wk gestation
	
	Assessment method:
	Fish intake measured via Food Use Questionnaire (2wk period) and 4-day food diary (2 consecutive weekdays and 2 weekend days)
	
	Outcomes and assessment methods:
	Infant novelty preference
	• FTII (Fagan Infant Test) at 5mo and 9mo
	  ○ Mean fixation duration
	  ○ Overall percentage novelty preference
	Infant visual recognition memory
	• VEXP (Visual Expectation Paradigm) at 5mo and 9mo
	  ○ Overall mean reaction time
	  ○ Overall percentage anticipatory saccades
	Infant/child development
	• BSID-II (Bayley Scales of Infant Development) at 9mo and 30mo
	  ○ Mental Developmental Index
	  ○ Psychomotor Development Index
	Child planning, inhibition, attention, and working memory
	• A-not-B test at 25mo:
	  ○ Overall percentage correct reaches
	  ○ Percentage of lose-stay errors
	• DSA (Delayed Spatial Alternation) at 25mo
	  ○ Overall percentage correct reaches
	  ○ Percentage of lose-stay errors
		Confounders accounted for:
		Child sex, child age, child birthweight, maternal age, parental education, maternal IQ, SES, prenatal MeHg exposure, blood DHA, blood AA, thyroid stimulating hormone (iodine status), iron stores, choline intake
		
		Limitations:
		• Several key confounders not accounted for: race/ethnicity, parity, gestational age, maternal anthropometrics, smoking, alcohol intake, non-fish exposure to n-3 PUFA
		• Study may be underpowered (sufficient power at n=250)

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Deroma, 2013[3]
Prospective Cohort Study, Italy
Baseline N=242 Analytic N=153 (Attrition: 37%)
 	
Participant characteristics:
• Maternal age: Mean=31.6, SD=5.0
• Female child: 50%
• Race/Ethnicity: NR
• SES: Maternal education at follow-up: Elementary school 1.3%, Middle school 30.9%, High school 52%, University 15.8%; Husband/in-mate education at follow-up: Elementary school 3.4%, Middle school 40.4%, High school 41.1%, University 15.1%; Married/common law-wife: 91.5%
• Parity: NR
• Pre-pregnancy BMI/wt at conception: NR
• GWG: NR
 	
Maternal seafood exposure:
• Fish intake during pregnancy: ≥2 svg/wk ~33%, Non-consumers 3.9%
• Seafood intake (Mean): 1.8 svg/wk
 	
Seafood nutrient exposure: NR
 	
Mercury exposure:
• Maternal hair THg (Mean): 1.33 ppm, Median: 0.93 ppm, range: 0.06-8.03
• Maternal hair THg (Mean): ~1375 ng/g
• Maternal hair MeHg (Mean): ~1000 ng/g
• Child hair THg at birth (Mean): ~1245 ng/g
• Child hair MeHg at birth (Mean): ~830 ng/g
• Child hair THg at 7y follow-up (Mean): ~730 ng/g
 	
Infant feeding practices: Breastfed: 89%
	Exposure:
	Maternal fresh and canned fish intake (svg/wk) during pregnancy assessed at 2-3mo postpartum
	
	Assessment method:
	54-item open-ended FFQ measured:
	• Fish (150 g)
	• Tuna, mackerel, and sardines in oil (80 g or 1 can)
	• Type, quantity, and origin of fish
	
	Outcomes and assessment methods:
	Cognition
	• WISC-III (Wechsler Intelligence Scale for Children III) at 7y
	  ○ Children's IQ
	  ○ Verbal IQ
	  ○ Performance IQ
		Confounders accounted for:
		Child sex, child age, child birthweight, maternal age, parental education, SES, smoking, alcohol intake, child's fish consumption at follow-up, breastfeeding, mother's age at delivery, maternal education, maternal alcohol intake during pregnancy, neuropsychological examiner, season of testing, THg ≥2000 ng/g in maternal hair at delivery, rental or free loan house, house size > 100m^2, living in Carlino in pregnancy, THg ≥2000 ng/g in child's hair at follow-up, fish intake of child at follow-up (svg/wk), canned fish intake of child, at follow-up (svg/wk)
		
		Limitations:
		• Several key confounders not accounted for: gestational age, parity, race/ethnicity, maternal anthropometrics, non-fish dietary exposure to n-3 PUFAs
		• Missing data handled differently based on participants' responses

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Furlong, 2018[4]
Prospective Cohort Study, Mount Sinai Children's Environmental Health Study, U.S.
Baseline N=404 Analytic N=162 (Attrition: 60%)
 	
Participant characteristics:
• Maternal age: <20y 30.9%, 20-24y 34.0%, ≥25y 35.2%
• Female child: NR
• Race/Ethnicity: Hispanic: 50.6%, Black/other: 31.9%, White: 18.5%
• SES: Maternal education: High school or less 73.3%, Some college or higher 26.7%; Marital status: Married 22.8%, Living with partner 22.8%; Single/divorced/widowed 54.3%
• Parity: 100% primiparous
• Pre-pregnancy BMI/wt at conception: NR
• GWG: NR
 	
Maternal seafood exposure during pregnancy:
• Canned fish consumption: <1x/wk ~87%, ≥1x/wk ~13%
 	
Seafood nutrient exposure: NR
 	
Mercury exposure: NR
 	
Infant feeding practices: NR
	Exposure:
	Maternal frequency of canned fish intake (times/wk) during pregnancy assessed at 3rd trimester
	
	Assessment method:
	Canned fish consumption measured via one question in a questionnaire
	
	Outcomes and assessment methods:
	Child neurodevelopment factor scores from the following assessments:
	• BRIEF (Behavior Rating Inventory of Executive Functioning) at 4-9y (parental report)
	• BASC (Behavioral Assessment System for Children) at 4-5y, 6y, and/or 7-9y (paternal report)
	• WPPSI-III (Wechsler Preschool and Primary Scales of Intelligence-III) at 6y
	• WISC-IV (Wechsler Intelligence Scales-IV) at 7-9y
	• Principal component analysis identified 7 factor solution using all tests:
	  ○ Impulsivity/externalizing
	  ○ Executive functioning
	  ○ Internalizing
	  ○ Perceptual reasoning
	  ○ Adaptability
	  ○ Processing speed
	  ○ Verbal intelligence
		Confounders accounted for:
		Child sex, child age, gestational age, parity, race/ethnicity, parental education, SES, smoking, alcohol intake, birth head circumference, HOME sub-scale scores of organization, learning materials, involvement, and variety
		
		Limitations:
		• Several key confounders not accounted for: child birthweight, maternal age, maternal anthropometrics, or non-fish dietary exposure to n-3 PUFA
		• Did not account for maternal mercury exposure
		• One non-validated question used to assess canned fish intake
		• BASC and BRIEF rely on parental report

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Gale, 2008[5]
Prospective Cohort Study, U.K.
Baseline N=559 Analytic N=217 (Attrition: 61%)
 	
Participant characteristics:
• Maternal age: Mean=27.0y, SD=4.7
• Female child: 47.9%
• Race/Ethnicity: White/Caucasian 100%
• SES: Educational qualifications: <A levels 58.1%, ≥A levels 41.9%; Social class: Manual 24.9%, Non-manual 75.1%
• Parity: 0 older siblings 55.8%, 1 older sibling 32.4%, ≥2 older siblings 12.6%
• Pre-pregnancy BMI/wt at conception: NR
• GWG: NR
 	
Maternal seafood exposure:
• Fish intake in early pregnancy: Never 8.76%, <1/wk 25.3%, 1-2/wk 47.0%, ≥3/wk 18.9%
• Oily fish intake in early pregnancy: Never 28.6%, <1/wk 46.1%, ≥1/wk 25.3%
• Fish intake in late pregnancy: Never 8.76%, <1/wk 19.4%, 1-2/wk 49.8%, ≥3/wk 22.1%
• Oily fish intake in late pregnancy: Never 32.3%, <1/wk 44.7%, ≥1/wk 23.0%
 	
Seafood nutrient exposure: NR
 	
Mercury exposure: NR
 	
Infant feeding practices:
• Duration of breastfeeding: Never 28.5%, <1mo 24.6%, 1-4mo 20.8%, >4mo 26.1%
	Exposure:
	Maternal seafood intake (total and oily fish) in early and late pregnancy assessed at 15wk and at 32wk gestation
	
	Assessment method:
	Seafood intake (including white fish, fish pie, fish fingers, fish in sauces, oily fish, and shell fish such as crab, prawns, and mussels) during early and late pregnancy measured via 100 item FFQ
	
	Outcomes and assessment methods:
	Child maladaptive behavior
	• SDQ (Strengths and Difficulties Questionnaire) at 9y (parental report)
	  ○ Total difficulties score
	  ○ Prosocial behavior scale
	  ○ Hyperactivity subscale
	  ○ Emotional symptoms subscale
	  ○ Conduct problems subscale
	  ○ Peer problems subscale
	• WASI (Wechsler Abbreviated Scale of Intelligence) at 9y
	  ○ Full scale IQ
	  ○ Performance IQ
	  ○ Verbal IQ
	
	Dichotomized (reference group vs the top 10-20% most adverse behavioral outcomes)
		Confounders accounted for:
		Child birthweight, child age, race/ethnicity, maternal age, parental education, SES, smoking, alcohol intake, duration of breastfeeding; family history of autism
		
		Limitations:
		• Several key confounders not accounted for: child sex, gestational age, parity, maternal anthropometrics, non-fish exposure to n-3 PUFA
		• Did not account for maternal mercury exposure
		• SDQ relies on parental report
		• Small sample size for several fish intake frequency groups likely limited statistical power
		• Different outcomes and intake groups used in analyses not clearly defined in the methods

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations
Hisada, 2017[8] **Prospective Cohort Study, Japan** Baseline N=315 Analytic N=88 (Attrition: 72%) **Participant characteristics:** • Maternal age: Mean=34.2y, SD=4.8; Median=34.0 • Female child: 55.9% • Race/Ethnicity: NR • SES: NR • Parity: 54% primiparous • Maternal BMI: Mean=20.6, SD=2.3; Median=20.3 • GWG: NR **Maternal seafood exposure:** NR **Seafood nutrient exposure:** NR **Mercury exposure:** NR **Infant feeding practices:** Breastfeeding: 79%	**Exposure:** Maternal seafood intake during pregnancy dichotomized as frequent eater vs less frequent eater; time period completed NR **Assessment method:** Seafood intake (including fish and shellfish) during pregnancy assessed via questionnaire survey of food consumption frequency **Outcomes and assessment methods:** Child development and behavior • KIDS (Kinder Infant Development Scale) at 18mo (parental report) ○ Physical motor subscale ○ Manipulation subscale ○ Receptive language subscale ○ Expressive language subscale ○ Language concepts subscale ○ Social relationships with children subscale ○ Social relationships with adults subscale ○ Discipline subscale ○ Feeding subscale	**Confounders accounted for:** Child sex, child age, child birthweight, gestational age, parity, maternal age, maternal anthropometrics, smoking, infant blood thyroid stimulating hormone 5d postpartum, breastfeeding, and ICCE score (Index of Child Care Environment) that assessed children's home environment **Limitations:** • Several key confounders not accounted for: race/ethnicity, parental education, alcohol, dietary supplement, dietary pattern, non-fish dietary exposure to n-3 PUFA • Did not account for maternal mercury exposure • Time period of seafood assessment is unknown • Average seafood intake and cut points used to distinguish less frequent or frequent eaters of seafood are not reported • KIDS relies on parental report • Cannot determine validity/reliability of fish assessment measure

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Hu, 2016[9]
Prospective Cohort Study, China
Baseline N=566 Analytic N=410 (Attrition: 28%)
 	
Participant characteristics:
• Maternal age: Mean: 28.03y, SD=4.5; ≤25y 31,7%, 25-30y 39.0%, >30y 29.3%
• Female child: 47.8%
• Race/Ethnicity: NR
• SES: Education: ≤High school 45.1%; Household monthly income (Renminbi): ≤3000 63.4%; 3000–5000 28.8%, >5000 7.8%
• Parity: 0 72.2%, ≥1 27.8%
• Pre-pregnancy BMI: Mean=21.84, SD=3.03, ≤18.5 9.8%, 18.5-23 62.0%, >23 28.3%
• GWG: Mean=15.94 kg, SD=6.66, ≤10 kg 20.2%, 10-20 kg 53.4%, >20 kg 26.3%
 	
Maternal seafood exposure during pregnancy:
• Total fish consumption: At least 1/wk 32.7%, At least 2/mo 39.5%, Monthly or less 27.8%
 	
Seafood nutrient exposure: NR
 	
Mercury exposure:
• Maternal whole blood mercury level: Geometric mean=0.72 µg/L (range:<LOD, 2.67), Mean=0.81 µg/L, SD=0.41
• Umbilical whole blood mercury level: Geometric mean=1.20 µg/L (range: 0.22, 4.55), Mean=1.37 µg/L, SD=0.73
 	
Infant feeding practices: NR
	Exposure:
	Maternal frequency of total fish intake during pregnancy assessed after delivery
	
	Assessment method:
	Maternal fish intake during pregnancy measured via questionnaire reconfirmed by nurses and missing information supplemented by telephone,
	
	Outcomes and assessment methods:
	Neurodevelopment
	• Chinese Pediatric Association-adapted GDS (Gesell Developmental Schedules) at 1y (Development quotient):
	  ○ Gross motor
	  ○ Fine motor
	  ○ Adaptive
	  ○ Language
	  ○ Social
		Confounders accounted for:
		Child sex, child age, child birthweight, gestational age, parity, maternal age, maternal anthropometrics, SES, smoking, alcohol, head circumference, frequency of total fish consumption, maternal blood lead, and maternal blood manganese
		
		Limitations:
		• Several key confounders not accounted for: race/ethnicity, non-fish n-3 PUFA
		• Did not account for maternal mercury exposure
		• Questionnaire used to assess fish intake not described or validated

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations
Spanish Childhood and Environment Project (INMA) Cohorts		

[Julvez, 2016][10]
Prospective Cohort Study, INMA, Spain
Baseline N=2,644 Analytic N=1,892 (Attrition: 28%)
 	
Participant characteristics:
• Maternal age: <31y 47.4%, ≥31y 52.6%
• Female child: 49.1%
• Race/Ethnicity: Born in: Spain 93.3%, Latin America 4.4%, Other place 2.3%
• SES: Education: Primary school or less 21.3%, Secondary school 41.6%, University or more 37.1%; Social class: Highly skilled 41.4%, Nonmanual 37.1%, Manual 21.5%
• Parity: 56.9% nulliparous, 43.1% parous
• Pre-pregnancy BMI/wt at conception: NR
• GWG: NR
 	
Maternal seafood exposure:
• Total seafood consumption (Mean): 498 g/wk, Median=454 g/wk
• Seafood non-consumers: 0.8%
 	
Seafood nutrient exposure: NR
 	
Mercury and other environmental exposures:
• Umbilical cord blood mercury level (N=1,541): <8.5 µg/L 48.4%, ≥8.5 µg/L 51.6%
• 1st trimester serum polychlorinated biphenyls (PCB): < 110.92 ng/g 49.0%, ≥110.92 ng/g 51.0%
• 1st trimester serum 2,2-bis(p-chlorophenyl)-1,1-dichloroethylene (DDE): <123.15 ng/g 50.2%, ≥123.15 ng/g 49.8%
 	
Infant feeding practices:
• Duration of breastfeeding (any): ≤24wk 55.3%, >24wk 44.7%
	Exposure:
	Maternal total seafood, large fatty fish, smaller fatty fish, lean fish, shellfish consumption (g/wk) assessed at 10-13wk and 28-32wk gestation
	
	Assessment method:
	Seafood intake (including large fatty fish, smaller fatty fish, lean fish, shellfish, and smoked/salted fish) measured via semi-quantitative FFQ (101 items) adapted for and validated in cohort
	
	Outcomes and assessment methods:
	Child neuropsychological development
	• BSID (Bayley Scales of Infant Development) at 14mo:
	  ○ Mental scale
	  ○ Psychomotor scale
	• MSCA (McCarthy Scales of Children's Abilities) at 5y:
	  ○ Verbal subscale
	  ○ Perceptual-performance subscale
	  ○ Memory subscale
	  ○ Quantitative subscale
	  ○ Motor subscale
	  ○ Executive function subscale
	Child Autism-spectrum traits
	• CAST (Childhood Asperger Syndrome Test) at 5y (parental report)
		Confounders accounted for:
		Child sex, child age, child birthweight, gestational age, parity, race/ethnicity, maternal age, maternal anthropometrics, parental education, SES, alcohol intake, non-fish dietary exposure to n-3 PUFA, Inclusion did not change results: study cohort (4 regions), total energy intake, quality of the test as recorded by the psychologist after examination, duration of breastfeeding, proxy verbal IQ, psychopath symptoms, main child minder-14mo, n-3, iodine and folate supplementation during pregnancy, 1st trimester serum PCB, 1st trimester serum DDE, cord blood mercury levels, n-6/n-3 ratio in cord blood levels, maternal m-6/n-3 intake ratio during pregnancy, maternal 25(OH)d3 plasma levels pregnancy, maternal iodine urine levels pregnancy
		
		Limitations:
		• Key confounder not accounted for: Family history of ASD in relevant analyses
		• Maternal mercury accounted for only in small subset of analyses
		• CAST relies on parental report
		• Seafood subtypes moderately correlated, therefore associations by subtype are not fully independent
		• Some analyses appear to be incompletely reported (e.g., only reporting 3rd trimester exposure results for MSCA)

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Llop, 2012[12]
Prospective Cohort Study, INMA, Spain
Baseline N=2,644 Analytic N=1,683 (Attrition: 36%)
 	
Participant characteristics:
• Maternal age: 30-34y 44.3%
• Female child: 47.6%
• Race/Ethnicity: Country of birth: Spain 92.2%, Other 7.8%
• SES: Education: Up to primary 22.2%, Secondary 41.1%, University 36.7%; Social class: Managers/technicians 33.4%, Skilled 25.7%, Semiskilled/unskilled 40.9%;
• Parity: 0 57.4%, 1 36.2%, ≥2 6.4%;
• Pre-pregnancy BMI: <18.5 4.0%, 18.5-<25 70.1%, 25-<30 19.0%, ≥30 6.9%;
• GWG: NR
 	
Maternal seafood exposure: NR
 	
Seafood nutrient exposure: NR
 	
Mercury exposure:
• Cord blood THg, Geometric Mean (95% CI): 8.4 µg/L (8.1, 8.7)
• Cord blood exceeding Environmental Protection Agency reference level for THg (6.4 µg/L): 65%
 	
Infant feeding practices:
• Breastfeeding: 0wk 14.7%, >0-16wk 23.8%, >16-24 15.5%, >24wk 46.0%
	Exposure:
	Maternal total seafood intake (g/wk) during pregnancy assessed at 1st and 3rd trimesters
	
	Assessment method:
	Seafood intake (including lean fish, large and small oily fish, canned tuna, shellfish, cephalopods, and other seafood) measured via a validated semi-quantitative 101-item FFQ, weekly intake of total seafood (sum of fish types) during pregnancy calculated
	
	Outcomes and assessment methods:
	Child neurodevelopment
	• BSID (Bayley Scales of Infant Development) at 14mo
	  ○ Mental Scale
	  ○ Psychomotor Scale
		Confounders accounted for:
		Child sex, child age, child birthweight, gestational age, parity, race/ethnicity, maternal age, maternal anthropometrics, parental education, SES (social class), smoking, cord blood THg, small-for-gestational-age length, attendance at a nursery, psychologist, season of delivery, calorie intake, cohort, cesarean, breastfeeding, main care provider
		
		Limitations:
		• Several key confounders not accounted for: alcohol intake, non-fish n-3 PUFA intake
		• No information provided on the magnitude or types of fish consumed
		• No cord blood available for ~24% of participants (excluded from analyses)

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Lederman, 2008[11]
Prospective Cohort Study, U.S.
Baseline N=329 Analytic N=151 (Attrition: 54%)
 	
Participant characteristics:
• Maternal age: NR
• Female child: 51%
• Race/Ethnicity: Asian: 27.2%, Black/African-American: 18.5%
• SES: Married or cohabiting ≥7 years: 81.5%; Material hardship: yes 6.6%; Per capita household income ($10k units): Mean=2.68, SD=1.75; Education: 14.8y, SD=3.5;
• Maternal IQ (Test of Non-verbal Intelligence): Mean=96.8, SD=14.6 Parity (≥1): 35.1%;
• Pre-pregnancy BMI: NR
• GWG: NR
 	
Maternal seafood exposure during pregnancy:
• Ate fish/seafood: 71.5%
 	
Seafood nutrient exposure: NR
 	
Mercury exposure:
• Maternal blood mercury: Mean=2.32 µg/L, Median=1.7 µg/L, SD=2.3, 95% CI: 2.01, 2.63
• Cord blood mercury: Mean= 7.82 µg/L, Median= 4.3 µg/L, SD=9.71, 95% CI: 6.67, 8.96
 	
Infant feeding practices:
• Child's proportion breast-fed, first year: Mean=0.287, SD=0.296
	Exposure:
	Maternal consumption of fish/seafood during pregnancy assessed during postpartum interview.
	
	Assessment method:
	Maternal fish/seafood consumption during pregnancy assessed via questionnaire and dichotomized as yes/no
	
	Outcomes and assessment methods:
	Child development
	• BSID-II (Bayley Scales of Infant Development) at 12mo, 24mo, and 36mo
	  ○ Mental Development Index
	  ○ Psychomotor Development Index
	• WPPSI-R (Wechsler Preschool and Primary Scale of Intelligence) at 48mo
	  ○ Full Scale IQ
	  ○ Performance IQ
	  ○ Verbal IQ
		Confounders accounted for:
		Child sex, child age, gestational age, race/ethnicity, maternal age, parental education, SES (per capita family income, marital status, material hardship), smoking, maternal IQ, proportion breast-feeding, Ln-cord mercury
		
		Limitations:
		• Several key confounders not accounted for: Child birthweight, parity, alcohol intake, non-fish exposure to n-3 PUFA, and maternal anthropometrics
		• Cannot determine validity/reliability of fish assessment measure
		• Fish/seafood intake dichotomized as none/any in analyses and the frequency of fish/seafood intake, levels of mercury in different fish/seafood, and quantity consumed per meal were not considered

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Mendez, 2009[13]
Prospective Cohort Study, Spain
Baseline N=482 Analytic N=392 (Attrition: 19%)
 	
Participant characteristics:
• Maternal age: Mean ~29y
• Female child: %
• Race/Ethnicity: NR
• SES: Education: Primary or less ~57%, Secondary ~27% Any higher ~16%
• Parity (no. of children): 0 ~49%, 1 ~39%, ≥2 ~12%
• Maternal weight status: Normal ~80.9%, Overweight/obese ~10.1%
• GWG: NR
 	
Maternal seafood exposure:
• Fish svg/wk during pregnancy, Mean (SD): 1.69 (1.5)
• Squid/shellfish svg/wk (mean): ~1.2; Fish: 57.7% of seafood intake
• Weekly fish intake during pregnancy:
• 1 or fewer 49.2% (including non-consumers 3.3%),
• >1-2 times 32.9%, >2-3 times 12.8%, >3 times 5.1%
 	
Seafood nutrient exposure: NR
 	
Mercury exposure: NR
 	
Infant feeding practices:
• Breastfeeding duration: < 6mo 62.2%, ≥6mo 37.8%
	Exposure:
	Maternal intake of fish and other seafood (octopus, squid and shellfish) during pregnancy assessed at 3mo postpartum
	
	Assessment method:
	42-item interviewer-administered, semi-quantitative, previously validated FFQ that included questions about fish, octopus, squid and shellfish consumption
	
	Outcomes and assessment methods: Cognitive development
	• MSCA (McCarthy Scales of Children's Abilities) at 4y:
	  ○ General cognition
	  ○ Perceptual-performance
	  ○ Memory
	  ○ Verbal
	  ○ Numeric
	  ○ Motor skills
		Confounders accounted for:
		Child sex, child age, child birthweight, gestational age, parity, maternal age, maternal anthropometrics, parental education, SES, smoking, alcohol, breastfeeding duration
		
		Limitations:
		• Two key confounders not accounted for: race/ethnicity, non-fish dietary exposure to n-3 PUFAs
		• Did not account for maternal mercury exposure

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations
Normia, 2019[15] **Prospective Cohort Study, Finland** Baseline N=238 Analytic N=19 (Attrition: 92%) **Participant characteristics:** • Maternal age: Mean=28.9y, SD=4.6 • Female child: 50% • Race/Ethnicity: NR • SES: NR • Parity: NR • Pre-pregnancy BMI: Mean=23.8, SD=3.8, 32% overweight • GWG: Mean=15.3 kg, SD=4.9 **Seafood exposure:** NR **Maternal seafood intake:** Mean=34g/d SD=40g; Frequency (Median)=3 times/wk (range: 0-6 times/wk) **Seafood nutrient exposure:** • Serum phospholipid fatty acid composition, Mean % of total fatty acids (SD): 3rd trimester: DHA 4.9 (1.1), EPA 1.6 (0.9); Child at 1mo: DHA 4.0 (0.9), EPA: 0.7 (0.3) **Mercury exposure:** NR **Infant feeding practices:** • Exclusive breastfeeding: Mean=13.8 wk, SD=6.7 • Total breastfeeding: Mean 41.2wk, SD=23.4	**Exposure:** Maternal frequency of fish consumption assessed 2wk prior to the 3rd trimester of pregnancy **Assessment method:** Assessed via questionnaire (not described) **Outcomes and assessment methods:** Neurodevelopment within the visual system • pVEP (Pattern-reversal visual evoked potentials) recordings at 2y	**Confounders accounted for:** Child sex, child age, child birth weight, gestational age, maternal anthropometrics, smoking, head circumference, mother's BMI or overweight status prior to pregnancy, GWG, blood glucose levels, presence of gestational diabetes, systolic or diastolic blood pressure, smoking, child duration of breastfeeding, birth height, gestational age **Limitations:** • Several key confounders not accounted for: parity, race/ethnicity, maternal age, parental education, SES, alcohol intake, or non-fish dietary exposure to n-3 PUFA • Did not account for maternal mercury exposure • Frequency of fish intake assessment tool not validated • Small sample size

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations
Project Viva Cohort Studies		
Oken, 2005[19] **Prospective Cohort Study, Project Viva, U.S.** Baseline N=211 Analytic N=135 (Attrition: 36%) **Participant characteristics:** • Maternal age: <30y 16%, 30-34y, 53%, ≥35y 31% • Female child: 51% • Race/Ethnicity: White/Caucasian: 82%, Other: 18% • SES: Education: Less than College graduate 20%, College or graduate degree 80% ; Marital status: Married or cohabitating 92%, Divorced or single 8% • Parity: NR • Pre-pregnancy BMI: NR • GWG: NR **Maternal seafood exposure during 2nd trimester:** • Total seafood intake (Mean): 1.2 svg/wk tuna, dark meat, white meat, and shellfish (range: 0–5.5 svg/wk) **Seafood nutrient exposure:** NR **Mercury exposure:** • Maternal hair mercury during 2nd trimester (Mean): 0.55 ppm, 95% CI: 0.02–2.38, Geometric mean=0.45 ppm • Maternal blood mercury levels >1.2 ppm: 10% subjects **Infant feeding practices:** • Breast-fed: 94% • Breast-fed until 6mo: ~50% • Breastfeeding duration: < 2mo: 19%, 2–4mo: 23%, ≥ 5mo: 58%	**Exposure:** Maternal total seafood intake (svg/wk) during the 2nd trimester of pregnancy assessed at 26-28wk gestation **Assessment method:** Weekly fish svg reported from validated FFQ (>140 items calibrated against blood levels of long-chain marine n-3 fatty acids); assessed intake of canned tuna fish; shrimp, lobster, scallops, and clams; dark meat fish; other fish **Outcomes and assessment methods:** Infant cognition • VRM (Visual recognition memory) at 6.5mo - percent novelty preference (average from 2 trials)	**Confounders accounted for:** Child sex, child age, child birthweight for gestational age, gestational age, race/ethnicity, maternal age, parental education, SES (marital status/cohabiting), smoking, alcohol intake, mercury intake, breastfeeding duration **Limitations:** • Several key confounders not accounted for: maternal BMI, smoking, parity, non-fish exposure to n-3 PUFA, alcohol intake • Potential bias due to missing data cannot be assessed

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Oken, 2008a[17]
Prospective Cohort Study, Project Viva, U.S.
Baseline N=1,579 Analytic N=341 (Attrition: 78%)
 	
Participant characteristics:
• Maternal age: Mean=32.6y, SD=4.7
• Female child: 51%
• Race/Ethnicity: White: 82%, Black: 6%, Hispanic: 2%, Other: 9%
• SES: Maternal education: High school 6%, Some college 14%, College graduate 40%, Graduate degree 41%; Paternal education: High school 23%, College graduate 41%, Graduate degree 36%; Partner status: Married/cohabiting 96%, Single 4%
• Parity (Birth order): 54% firstborn, 46% not firstborn
• Pre-pregnancy BMI: <25 70%, 25-30 20%, >30 10%
• GWG: NR
 	
Maternal seafood exposure during 2nd trimester:
• Fish intake (Mean): 1.5 svg/wk, SD=1.4 (range 0–7.5 svg/wk)
• Fish intake: Never 14%, ≤2 svg/wk 74%, >2 svg/wk 12%
 	
Seafood nutrient exposure:
• Maternal 2nd trimester intake of DHA and EPA from fish (Mean): 128 mg/d, SD=128;
• Maternal 2nd trimester intake of DHA and EPA from fish by intake category (Means): Never 0 mg/d SD=0, ≤2 svg/d 122 mg/d SD=97, >2 svg/d 318 mg/d SD=160
 	
Mercury exposure:
• Maternal 2nd trimester erythrocyte mercury (Mean): 3.8 ng/g, SD=3.8 (range: 0.03-21.9 ng/g)
 	
Infant feeding practices:
• Breastfeeding: Mean=7.0mo, SD=4.5
	Exposure:
	Maternal 2nd trimester seafood intake (svg/wk) assessed at 26-28wk gestation
	
	Assessment method:
	Seafood intake (including canned tuna fish, shrimp, lobster, scallops, and clams, dark meat fish, and other fish) measured via a validated semiquantitative FFQ (>140 items) modified for pregnancy and calibrated against erythrocyte levels of n-3 fatty acids
	
	Outcomes and assessment methods:
	Child receptive vocabulary
	• PPVT (Peabody Picture Vocabulary Test) at 3y
	Child visual motor development
	• WRAVMA (Wide Range Assessment of Visual Motor Ability) at 3y:
	  ○ Total standard score
	  ○ Visual-spatial subscale (matching test)
	  ○ Visual-motor subscale (drawing test)
	  ○ Fine motor subscale (pegboard test)
		Confounders accounted for:
		Child sex, child age, child birthweight (fetal growth), gestational age, race/ethnicity, maternal age, maternal anthropometrics, parental education (maternal and paternal), SES (marital status), smoking, alcohol intake, duration of breastfeeding, child primary language, maternal PPVT score
		
		Limitations:
		• Several key confounders not accounted for: Parity
		• Analyses categorized by seafood and Hg resulted in small N for some categories

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Oken, 2016[18]
Prospective Cohort Study, Project Viva, U.S.
Baseline N=2,128 Analytic N=1,068 (Attrition: 50%)
 	
Participant characteristics:
• Maternal age: Mean=32.2y, SD=5.3 (range: 15.3-44.9y)
• Female child: 50%
• Race/Ethnicity: White: 69%, Black: 16%, Hispanic: 6%, Asian: 5%, Other: 4%
• SES: College graduate: Yes 69%, No 31%; Married/cohabitating: Yes 92%, No 8% ; Annual household income >$70,000: Yes 62%, No 38%; Partner college graduate: Yes 64%, No 36%
• Parity: Nulliparous 48%
• Pre-pregnancy BMI: Mean=24.6, SD=5.1 (range: 16.2-48.5);
• GWG: NR
 	
Maternal seafood exposure:
• Fish intake mid-pregnancy during the previous 3mo (Mean): 1.7 svg/wk, SD=1.5 (range: 0.0-12.0 svg/wk)
• Fish intake mid-pregnancy during the previous 3mo: 0 svg/wk 12%, >0-<3.0 svg/wk 75%, ≥3 svg/wk 13%
 	
Seafood nutrient exposure:
• Maternal DHA+EPA intake mid-pregnancy (Mean): 165 mg/d, SD=158 (range: 0-2060 mg/d);
• Maternal plasma DHA+EPA mid-pregnancy (Mean, N=872): 98.4 µg/ml, SD=41.8 (range: 16.8-327.1 µg/ml);
• Maternal erythrocyte selenium mid-pregnancy (Mean, N=872): 205.6 ng/ml, SD=34.6 (range: 44.3-380.3 ng/ml)
 	
Mercury exposure:
• Maternal erythrocyte mercury (Mean, N=872): 4.0 ng/g, SD=3.6 (range: 0-38.2 ng/g)
 	
Infant feeding practices:
• Breastfeeding duration: Mean=6.4mo, SD=4.6 (range: 0-12mo)
	Exposure:
	Maternal seafood intake (svg/wk) during pregnancy assessed at 27.9wk gestation (2nd trimester) and post-delivery (3rd trimester)
	
	Assessment method:
	Seafood intake (including canned tuna fish, shrimp, lobster, scallops, clams, dark meat fish such [e.g., mackerel, salmon, sardines, bluefish, and swordfish], and other fish [e.g., cod, haddock, halibut]) during mid-pregnancy and post delivery measured via validated 140 item semi-quantitative FFQ
	
	Outcomes and assessment methods:
	Child visual motor abilities
	• WRAVMA (Wide Range Assessment of Visual Motor Abilities) at ~6-11y
	  ○ Drawing Scale
	Child visual memory
	• WRAML (Wide Range Assessment of Memory and Learning) at ~6-11y
	  ○ Visual Memory Summary Score
	  ○ Picture Memory
	  ○ Design Memory Subtests
	Child IQ, Fluid reasoning, and Crystallized ability
	• KBIT-II (Kaufman Brief Intelligence Test) at ~6-11y
	  ○ Verbal IQ subtest
	  ○ Nonverbal IQ subtest
		Confounders accounted for:
		Child sex, child age, child birthweight, gestational age, parity, race/ethnicity, maternal and partner education, maternal IQ, SES (HOME score), smoking, alcohol, breastfeeding duration, child primary language, erythrocyte mercury (subsample with blood biomarker data only), maternal use of recreational drugs during pregnancy
		
		Limitations:
		• Several key confounders not accounted for: maternal age, maternal anthropometrics, non-fish n-3 PUFA exposure
		• Maternal mercury accounted for only in small subset of analyses

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Oken, 2008b[16]
Prospective Cohort Study, Danish National Birth Cohort (DNBC), Denmark
Baseline N=101,042 Analytic N=25,446 (Attrition: 75%)
 	
Participant characteristics:
• Maternal age: Mean=29.3y, SD=4.1
• Female child: 49.7%
• Race/Ethnicity: NR
• SES: high 23.3%, medium 32.5%, skilled 28.0%, unskilled 10.1%, unemployed 1.2%, student 4.8%; Unmarried: 0.9%; Maternal education: <9th grade 0.3%, 9th grade 6.5%, 10th grade 25.9%, graduated from 2-y high school (HS, standard duration of Danish HS) 13.7%, graduated from HS 53.7%
• Parity: 47.5% nulliparous
• Pre-pregnancy BMI: ≤18.5 4.1%, >18.5 to 25 68.0%, ≥25 to <30 19.7%, ≥30 to <35 6.1%, ≥35 to <40 1.6%, ≥40 0.6%
• GWG: NR
 	
Maternal seafood exposure:
• Fish intake (mean): 26.6 g/d, SD=22.7;
• Fish intake: lowest quintile mean=5.4 g/d (range: 0-10.5 g/d), middle quintile mean=22.3 g/d (range: 18.2-26.8 g/d), highest quintile mean=58.6 g/d (range: 39.4-493.9 g/d);
• Fish intake: 0 svg/wk 2.8%, 1-2 svg/wk 86.3%, ≥3 svg/wk 11.0%;
• Most frequently consumed fish species: cod, plaice, salmon, herring, mackerel (85% of total seafood intake in DNBC)
 	
Seafood nutrient exposure: NR
 	
Mercury exposure:
• Mercury content of most frequently consumed fish species in DNBC (from Danish food monitoring program, Median): 0.034-0.049 ppm
 	
Infant feeding practices:
• Breastfeeding duration: Mean=7.9mo, SD=4.6
	Exposure:
	Maternal fish intake (including fish as a main meal and fish with bread) in the month preceding the 25wk gestation; analysis stratified by breastfeeding duration
	
	Assessment method:
	Measured via a validated, self-administered semi-quantitative FFQ (>360 items, modified from Danish Cancer Registry FFQ, validated against 7-d weighed food diaries and blood biomarkers)
	
	Outcomes and assessment methods:
	Child milestone attainment
	• Maternal report on 12 questions regarding motor, social, and cognitive milestones (e.g., child could drink from a cup, child could write or draw, age that child could first sit unsupported, etc.) at 18mo
	  ○ Total developmental scale
	  ○ Overlapping subscales for motor milestones and social or cognitive milestones
	Infant milestone attainment
	• Maternal report on 13 yes-no questions regarding motor, social, and cognitive milestones (e.g., child could hold up head, child could express dislikes, child could crawl, etc.) at 6mo
	  ○ Total developmental scale
	  ○ Overlapping subscales for motor milestones and social or cognitive milestones
		Confounders accounted for:
		Child sex, Child age, Child birthweight, Gestational age, Parity, Maternal age, Maternal anthropometrics, Parental education, SES (including parental education), Smoking, Alcohol intake, Postpartum depression
		
		Limitations:
		• Several key confounders not accounted for: non-fish dietary exposure of n-3 PUFA, race/ethnicity
		• Did not adjust for maternal mercury exposure
		• Did not use a validated test of child development
		• Developmental milestones assessment relies on parental report

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations
Public health impact of long-term, low-level mixed element exposure in susceptible population strata (PHIME) Cohort Studies		

Valent, 2013[22]
Prospective Cohort Study, PHIME Italian subcohort, Italy
Baseline N=767 Analytic N=606 (Attrition: 21%)
 	
Participant characteristics:
• Maternal age: Mean=33.3y, SD=4.3, Median=33
• Female child: 49.3%
• Race/Ethnicity: Country of birth of mother: Italy 92.9%
• SES: Educational level: Elementary school 0.8%, Middle school 15.7%, High school 48.3%, University degree 34.8%; Employed 83.8%, Number of children living in home: 1 55.9%, 2 33.0%, 3 6.4%, >3 1.8%
• Parity: NR
• Pre-pregnancy BMI: Mean=23.3, SD=14.5, Median=22.2
• GWG: Mean=13.3 kg, SD=4.2, Median=13 kg
 	
Maternal seafood exposure during pregnancy:
• Fresh or frozen fish: Mean=1.06 svg/wk, Median=0.92 svg/wk, SD=0.99 (range: 0-6 svg/wk)
• Fresh, frozen, and canned fish: Mean=1.69 svg/wk, Median=1.38 svg/wk, SD=1.30 (range: 0-7 svg/wk)
• Fish, mollusk, and crustacean: Mean=2.33 svg/wk, Median=1.84 svg/wk, SD=1.71 (range: 0-11 svg/wk)
• Top 3 most frequently consumed fish species in cohort (Mean):
  • Tuna, 0.64 x/wk
  • Sea Bass, 0.34 x/wk
  • Gilt-Head Bream, 0.32 x/wk
 	
Seafood nutrient exposure:
• Maternal serum EPA (N=589): Mean=0.039 mg/mL, SD=0.035, Median=0.026 mg/mL, Q1=0.024, Q3=0.034 (range: 0.018-0.200 mg/mL)
• Maternal serum DHA (N=589): Mean=0.045 mg/mL, SD=0.029, Median=0.036 mg/mL, Q1=0.018, Q3=0.064 (range: 0.014-0.152 mg/mL)
	Exposure:
	Maternal overall seafood intake (svg/wk) during pregnancy assessed soon after delivery
	
	Assessment method:
	Seafood intake (including fish, crustaceans, and mollusks) during pregnancy measured via 138-item FFQ adapted from a validated Italian FFQ
	
	Outcomes and assessment methods:
	Child neurodevelopment
	• BSID-III (Bayley Scales of Infant Development) at 18mo
	  ○ Cognitive
	  ○ Language
	  ○ Motor
	  ○ Social-emotional
	  ○ Adaptive behavior scores
		Confounders accounted for:
		Child sex, child age, child birthweight, gestational age, maternal age, maternal anthropometrics (GWG), parental education, maternal IQ, SES, number of children in home, smoking, alcohol intake, breastfeeding history, child intake of fish until age 18mo, daycare attendance at age 18mo, FAs in maternal serum and proportion of PUFAs and/or THg in maternal hair depending on model
		
		Limitations:
		• Several key confounders not accounted for: race/ethnicity, parity, non-fish n-3 PUFA exposure
		
		Limited reporting of associations between fish intake and child development

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations
• Maternal serum total n-3 PUFA (N=589): Mean=0.154 mg/mL, SD=0.054, Median=0.136 mg/mL, Q1=0.114, Q3=0.176 (range: 0.072-0.406 mg/mL) **Mercury exposure:** • Maternal hair THg: Mean=1061 ng/g, SD=1028, Median=788 ng/g, Q1=481, Q3=1281 (range: 17-13520 ng/g) • Cord blood THg (N=457): Mean=5.54 ng/g, SD=4.83, Median=3.97 ng/g, Q1=2.40, Q3=7.02 (range: 0.12-32.76 ng/g) • Breast milk THg (N=492): Mean=0.33 ng/g, SD=1.31, Median=0.18 ng/g, Q1=0.11, Q3=0.28 (range: 0-28.30 ng/g) **Infant feeding practices:** NR		

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Barbone, 2019[26]
Prospective Cohort Study, PHIME cohort, Croatia, Greece, Italy, Slovenia
Baseline N=2189 Analytic N=1308 (Attrition: 40%)
 	
Participant characteristics:
• Maternal age: Mean=31.4y, SD=5.1, Median=32
• Female child: 51.4%
• Race/Ethnicity: NR
• SES: Educational level: Elementary and middle school 20.3%, High school 43.0%, University degree 36.7%; Employed 78%, Number of additional children living in home: None 52.7%, One or more 47.3%
• Parity: NR
• Pre-pregnancy BMI: Mean=23.2, SD=4.5, Median=22.5
• GWG: Mean=13.9 kg, SD=5.4, Median=14 kg
 	
Maternal seafood exposure during pregnancy:
• Seafood consumption/wk: Mean=1.4 svg/wk, SD=1.2, Median=1 svg/wk
 	
Mercury exposure:
• Maternal hair THg: Mean=997.0 ng/g, SD=1035.1, Median=704 ng/g
• Maternal blood THg: Mean=3.2 ng/g, SD=3.4, Median=2.4 ng/g
• Cord blood THg: Mean=5.2 ng/g, SD=5.0, Median=3.6 ng/g
• Breast milk THg: Mean=0.4 ng/g, SD=1.2, Median=0.2 ng/g
 	
Infant feeding practices:
• Breastfeeding: Mean=8.4mo, SD=6, Median=8mo
	Exposure:
	Maternal overall seafood intake (svg/wk) during pregnancy assessed soon after delivery
	
	Assessment method:
	Frequency of 150 g servings of seafood intake (including fish, crustaceans, and mollusks) during pregnancy measured via 138-item FFQ adapted from a validated Italian FFQ
	
	Outcomes and assessment methods:
	Child neurodevelopment
	• BSID-III (Bayley Scales of Infant and Toddler Development) at 18mo
	  ○ Cognitive
	  ○ Language
	  ○ Motor
	  ○ Receptive communication scaled score
	  ○ Expressive communication scaled score
	  ○ Fine motor scaled score
	  ○ Gross motor scaled score
		Confounders accounted for:
		Child age, SES
		
		Limitations:
		• Several key confounders not accounted for: Child sex, race/ethnicity, parity, child birthweight, gestational age, maternal anthropometrics, parental education, smoking, alcohol intake, non-fish n-3 PUFA exposure

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Sagiv, 2012[20]
Prospective Cohort Study, The New Bedford Cohort, U.S.
Baseline N=788 Analytic N=421 (Attrition: 47%)
 	
Participant characteristics:
• Maternal age: <20y 13.3%, 20-29y 49.6%, 30-34y 23.8%, 35y+ 13.3%
• Female child: 49.6%
• Race/Ethnicity (Child): White: 74.2%, Non-white: 25.8%
• SES: Maternal education at child's 8y exam: <12th grade 8.2%, HS graduate 30.5%, Some college 61.3%; Annual household income at child's 8y exam: <$20,000 17.8%, $20-39,999 27.0%, ≥$40,000 55.2%; Maternal marital status at 8y exam: Married 61.0%, Unmarried 39.0%
• Parity: NR
• Pre-pregnancy BMI: NR
• GWG: NR
 	
Maternal seafood exposure:
• Fish intake: Mean=3.7 svg/wk, SD=3.9, Median=2.3 (range: 0-22.6 svg/wk); >2 svg/wk 52.5%, ≤2 svg/wk 47.5%
• Local fish intake during pregnancy: No 88.9%, Yes 11.1%
 	
Seafood nutrient exposure:
• Maternal n-3 intake (Mean): 28.4 g/mo, SD=14.9
 	
Mercury exposure:
• Maternal hair mercury (~10d postpartum, Mean): 0.62 µg/g, SD=0.57, Median=0.45 (range: 0.03-5.14 µg/g)
 	
Infant feeding practices: NR
	Exposure:
	Maternal total seafood intake (svg/wk) during pregnancy assessed shortly after birth
	
	Assessment method:
	Seafood intake (including dark fish, e.g., salmon, mackerel, bluefish, swordfish; tuna including canned tuna; shellfish, e.g., lobster, clams; eel; other fish) assessed via FFQ
	
	Outcomes and assessment methods:
	Risk of ADHD symptoms
	• CRS-T (Conners' Rating Scale-Teachers) at 8y (parental report)
	  ○ Total (subtypes combined) Subscale
	  ○ Inattentive Subscale
	  ○ Hyperactive-impulsive Subscale
	Cognitive performance
	• CPT (Neurobehavioral Evaluation System 2 Continuous Performance Test) at 8y
	  ○ Mean response time
	  ○ Response time variability
	  ○ Errors of omission
	  ○ Errors of commission
	Intellectual abilities
	• WISC-III (Wechsler Intelligence Scale for Children - Third Edition) at 8y
	  ○ Processing speed subscale
	  ○ Freedom from distractibility subscale
		Confounders accounted for:
		Child sex, child age, race/ethnicity, maternal age, parental education, SES, smoking, alcohol intake, illicit drug use, depression symptoms; assessed sensitivity of results to ADHD medication use, 2y blood lead levels, cord serum PCB levels
		
		Limitations:
		• Several key confounders not accounted for: child birth weight, gestational age, parity, maternal anthropometrics, family history of neurocognitive disorders, non-fish dietary exposure to n-3 PUFA
		• CRS-T relies on parental report
		• Cannot determine validity/reliability of fish assessment measure

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations
Steenweg-de Graaff, 2016[21] **Prospective Cohort Study, Generation R Study, Netherlands** Baseline N=6,611 Analytic N=3,802 (Attrition: 42%) **Participant characteristics:** • Maternal age: ~31y • Female child: ~50% • Race/Ethnicity: Dutch: ~59%, Non-Dutch: ~41% • SES: Family income: >2,000 euro (~$2230/mo): ~70%; Cohabitation: 90%; Education: Higher 51%, Secondary or primary 49%; Paternal education: Higher ~55%, Secondary or primary ~45% • Parity: ~58% primiparous, ~42% multiparous • Pre-pregnancy BMI: ~23.5 • GWG: NR **Maternal seafood exposure:** • Fish intake: Mean=11.5g/d, Range=1.4-50.5 **Seafood nutrient exposure:** NR **Mercury exposure:** NR **Infant feeding practices:** • Breastfeeding (partial) until 6mo: yes 33%	**Exposure:** Maternal seafood intake in early pregnancy assessed at 14wk **Assessment method:** Fish intake (g/d) over the past 3 months including all types of fish consumed, assessed using a modified, validated semiquantitative FFQ **Outcomes and assessment methods:** Child nonverbal IQ • SON-R (Snijders-Oomen Niet-verbale Intelligentietest – Revisie) at 6y ○ Nonverbal IQ score (combined spatial visualization and abstract reasoning abilities) Child autistic traits (parental report) • SRS (Social Responsiveness Scale) at 6y	**Confounders accounted for:** Child sex, child age, child birthweight, gestational age, parity, race/ethnicity, maternal age, pre-pregnancy BMI, parental education, SES, smoking, alcohol intake, maternal daily caloric intake, maternal IQ, national origin, psychopathology score in mid-pregnancy, child daycare attendance, child IQ, parity, marital status, pregnancy planning, child gestational age and weight at birth, breastfeeding status at 6 months, and paternal age and body mass index **Limitations:** • One key confounder not accounted for: non-fish dietary exposure of n-3 PUFA • Did not account for maternal mercury exposure • SRS relies on parental report • Did not use clinical diagnoses of autism

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations
Vejrup, 2018[23] **Prospective cohort study; Mother and Child Cohort Study (*MoBa*), Norway** Baseline N=95,200 Analytic N=38,297 (Attrition: 60%) **Participant characteristics:** • Female child: 49% • Race/ethnicity: NR • Maternal SES: College 1-3 y or higher 75.2%; Married or cohabitating: 97% • Maternal age at delivery (Mean): 30.7y, SD=4.4 • Nulliparous: 48.3% • Pre-pregnancy BMI (Mean): 23.9, SD=4.1 • GWG: NR **Maternal seafood exposure:** • Fish intake (Median): 25.8 g/d, SD=19.0 • Total seafood intake (Median): 31.0 g/d, SD=20.9 **Seafood nutrient exposure:** • Maternal blood selenium concentration (subsample N: 2239) (Median): 102.3 µg/L, SD=22.9 **Mercury exposure:** • Maternal mercury intake (Median): 1.48 µg/d, SD=0.97 • Maternal blood mercury concentration (subsample N: 2239) (Median): 1.0 µg/L, SD=0.9 **Infant feeding practices:** • Duration any breastfeeding (Mean): 10.2mo, SD=4.4	**Exposure:** Maternal total seafood intake (g/wk) assessed at 22wk gestation **Assessment method:** Semi-quantitative FFQ validated in the MoBa sample to estimate intake of fish, shellfish and crustaceans from beginning of pregnancy **Outcomes and assessment methods:** Child language and communication skills (parental report) • ASQ (Norwegian Ages and Stages) Communication Scale at 5y • SLAS (Speech and Language Assessment Scale) at 5y • Language 20 (Twenty Statements about Language-Related Difficulties List) at 5y	**Confounders accounted for:** Child age, maternal age, maternal education, parity, pre-pregnancy BMI, SCL-5 (maternal anxiety/depression symptoms), maternal intake of EPA and DHA from supplements, total energy intake, smoking, alcohol intake, breastfeeding, prenatal exposure to PCB and dioxin-like compounds, maternal blood selenium*, maternal blood mercury* *In subsample analyses restricted to those with blood samples **Limitations:** • Several key confounders not accounted for: race/ethnicity, SES, gestational age, child birthweight, child sex • Maternal mercury accounted for only in small subset of participants • ASQ, SLAS, and Language 20 relies on parental report • Seafood intake lower in subsample with maternal mercury exposure data (RoB due to missing data)

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations

Xu, 2016[25]
Prospective Cohort Study, HOME study, U.S.
Baseline N=468 Analytic N=344 (Attrition: 26%)
 	
Participant characteristics:
• Maternal age: Mean=30y, SD=5.8
• Female child: 53%
• Race/Ethnicity: White, non-Hispanic: 63%, Black, non-Hispanic: 30%, Other: 7%
• SES: Education: ≤ High school or GED 22%, Some college or college graduate 56%, Graduate or professional school 22%; Household income (Median): $55K (25th %ile: $27K, 75th %ile: $85K); Marital status: Married 67%, Not married, living with someone, 13%, Not married, living alone 20%
• Parity: NR
• Pre-pregnancy BMI: NR
• GWG: NR
 	
Maternal seafood exposure:
• Fish-containing meals during pregnancy (Median): 13, IQR: 6-17
• Fish intake during conception to ~20wk gestation:
  • Any fish intake: 84%
  • Fish intake 1-3x/month or less: 63%
  • Tuna intake: 60%
  • Shellfish intake: 59%
  • Salmon intake: 42%
  • Local river or lake fish intake: 7%
 	
Seafood nutrient exposure: NR
 	
Mercury exposure:
• Maternal whole blood THg, Geometric mean (95% CI):
  • 16wk gestation: 0.65 µg/L (0.59, 0.71), range: 0.14-8.3 µg/L
  • 26wk gestation: 0.56 µg/L (0.50, 0.62), range: 0.14-6.7 µg/L
  • At delivery: 0.60 µg/L (0.55, 0.66), range: 0.14-4.3 µg/L
  • Over gestation: 0.64 µg/L (0.59, 0.75), range: 0.14-6.4 µg/L
	Exposure:
	Maternal fish intake during entire pregnancy assessed at 16wk gestation and 5wk postpartum.
	
	Assessment method:
	Fish intake (including salmon, tuna, shellfish, lake trout, mackerel, swordfish, tilefish, shark) during pregnancy measured via questionnaires completed; total fish consumption was calculated by summing all fish types from both surveys.
	
	Outcomes and assessment methods:
	Infant neurobehavior
	• NNNS (NICU Network Neurobehavioral Scale) at 5wk, 13 subscales but reported on 3 subscales including:
	  ○ Attention
	  ○ Need for special handling
	  ○ Asymmetry
		Confounders accounted for:
		Child sex, child age, parental education, SES, alcohol intake, total energy intake (prenatal)
		
		Limitations:
		• Several key confounders not accounted for: child birth weight, gestational age, parity, race/ethnicity, maternal age, maternal anthropometrics, smoking, non-fish dietary exposure to n-3
		• Cannot determine validity/reliability of fish assessment measure

Study and Population Characteristics	Exposure and Outcomes	Confounders and Study Limitations
• Cord whole blood THg, Geometric mean (95% CI): 0.72 µg/L (0.64, 0.81), range: 0.14-14.3 µg/L **Infant feeding practices:** • Being breastfed at least 1wk: 78%		

[iv] 1 oz = 28.3 grams
[v] Abbreviations: AA – arachidonic acid, CI – confidence interval, d – day(s), DDE – 2,2-bis(p-chlorophenyl)-1,1-dichloroethylene, FFQ – food frequency questionnaire, GWG – gestational weight gain, IQR – interquartile range, MeHg – methyl mercury, mo – month(s), NR – not reported, n-3 – omega-3, PCB – polychlorinated biphenyls, ppm – parts per million, SD – standard deviation, SES – socioeconomic status, svg – serving(s), THg – total mercury, wk – week(s), wt – weight, x – time(s), y – year(s), %ile -- percentile

Table 2. Results from studies that examined the relationship between seafood consumption during pregnancy and neurocognitive development in the child (Developmental Domains)[vi,vii]

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Avon Longitudinal Study of Parents and Children (ALSPAC)		
Williams, 2001[24] **Prospective Cohort Study** **ALSPAC; U.K.** ***Summary:*** *Mothers who ate oily fish during pregnancy were more likely to have children who achieved foveal stereoacuity than were mothers who never ate oily fish. White fish and shellfish were not associated with achievement of foveal stereoacuity.*	Maternal fish intake at 32wk gestation: No (N~101) vs Yes (N~342)	*Achievement of foveal stereoacuity indicates maturation to adult or high-grade stereoacuity and reflects greater maturity of the visual cortex* **Proportion of 3 grades of stereoacuity at 3.5y** Foveal stereo: Yes (33.9%) vs No (6.4%) Macular stereo: Yes (52.1%) vs No (54.5%) Peripheral stereo: Yes (14.0%) vs No (9.1%) **Group differences, P=0.046, unadjusted analysis**
	Maternal oily fish intake during pregnancy: No (Ref, N~172) vs Yes (N~271)	**Foveal stereoacuity at 3.5y** No (Ref) vs Yes: OR: 1.57, 95% CI: 1.00, 2.45
	Maternal oily fish intake during pregnancy: No (Ref, N=NR) vs Yes (N=NR) Sub-analysis of mothers who never breastfed (N=101)	**Foveal stereoacuity at 3.5y** No (Ref) vs Yes: OR: 1.26, 95% CI: 0.47, 3.35
	Maternal white fish intake during pregnancy: No (N~77) vs Yes (N~366)	**Foveal stereoacuity at 3.5y, OR** White fish intake did not significantly improve fit of the model and was not retained (Data NR)
	Maternal shellfish intake during pregnancy: No (N~335) vs Yes (N~108)	**Foveal stereoacuity at 3.5y, OR** Shellfish intake did not significantly improve fit of the model and was not retained (Data NR)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Daniels, 2004[1] **Prospective Cohort Study** **ALSPAC; U.K.** ***Summary:*** *Maternal fish intake during pregnancy associated with modestly higher scores on the ALSPAC adaptations of the MCDI vocabulary and social activity subscales and the DDST total score and language subscale.*	Maternal fish intake during pregnancy: Rarely/never (0 oz/wk; Ref) vs 1 meal/2wk (2.25 oz/wk) vs 1-3 meals/wk (9 oz/wk) vs 4+ meals/wk (18 oz/wk) Test for trend assesses change per oz/wk DDST: Total score (N=7116), Language (N=7135), Social (N=7127) MCDI: Vocabulary comprehension (N=7054), Social activity (N=7329)	*Higher scores on the ALSPAC adaptation of the MacArthur Communicative Development Inventory (MCDI) indicate better child performance* **ALSPAC-adapted MCDI Vocabulary comprehension at 15mo, Mean raw scores** Rarely/never: 68.2, 95% CI: 66.3, 70.5 1 meal/2wk: 70.9, 95% CI: 69.0, 72.9 1-3 meals/wk: 73.0, 95% CI: 71.3, 74.8 4+ meals/wk: 71.9, 95% CI: 70.5, 73.8 **Test for trend: B: 0.11, SE: 0.05, P=0.03** **ALSPAC-adapted MCDI Social activity at 15mo, Mean raw scores** Rarely/never: 16.4, 95% CI: 16.0, 16.7 1 meal/2wk: 17.0, 95% CI: 16.6, 17.3 1-3 meals/wk: 17.1, 95% CI: 16.8, 17.4 4+ meals/wk: 17.2, 95% CI: 16.9, 17.5 **Test for trend: B: 0.03, SE: 0.009, P=0.002**
		ALSPAC-adapted MCDI Vocabulary comprehension at 15mo, OR for low test score (low 15 %ile) Rarely/never (Ref) vs 1 meal/2wk: OR: 0.8, 95% CI: 0.6, 1.1 Rarely/never (Ref) vs 1-3 meals/wk: OR: 0.8, 95% CI: 0.6, 1.0 Rarely/never (Ref) vs 4+ meals/wk: OR: 0.9, 95% CI: 0.7, 1.2 Test for trend: B: 0.0003, SE: 0.0006, P=0.9 **ALSPAC-adapted MCDI Social activity at 15mo, OR for low test score (low 15 %ile)** Rarely/never (Ref) vs 1 meal/2wk: OR: 0.8, 95% CI: 0.6, 1.1 **Rarely/never (Ref) vs 1-3 meals/wk: OR: 0.6, 95% CI: 0.5, 0.8** **Rarely/never (Ref) vs 4+ meals/wk: OR: 0.7, 95% CI: 0.5, 0.9** **Test for trend: B: -0.02, SE: 0.007, P=0.02**

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Daniels, 2004 **Prospective Cohort Study; ALSPAC; U.K.** **(Continued)**	Maternal <u>fish</u> intake during pregnancy: Rarely/never (0 oz/wk; Ref) vs 1 meal/2wk (2.25 oz/wk) vs 1-3 meals/wk (9 oz/wk) vs 4+ meals/wk (18 oz/wk) Test for trend assesses change per oz/wk DDST: Total score (N=7116), Language (N=7135), Social (N=7127) MCDI: Vocabulary comprehension (N=7054), Social activity (N=7329)	**ALSPAC-adapted MCDI Vocabulary comprehension at 15mo, OR for high test score (top 15 %ile)** **Rarely/never (Ref) vs 1 meal/2wk: OR: 1.3, 95% CI: 1.0, 1.8** **Rarely/never (Ref) vs 1-3 meals/wk: OR: 1.5, 95% CI: 1.1, 2.0** **Rarely/never (Ref) vs 4+ meals/wk: OR: 1.5, 95% CI: 1.1, 2.0** Test for trend: B: 0.01, SE: 0.006, P=0.05 **ALSPAC-adapted MCDI Social activity at 15mo, OR for high test score (top 15 %ile)** **Rarely/never (Ref) vs 1 meal/2wk: OR: 1.6, 95% CI: 1.2, 2.2** **Rarely/never (Ref) vs 1-3 meals/wk: OR: 1.7, 95% CI: 1.3, 2.2** **Rarely/never (Ref) vs 4+ meals/wk: OR: 1.8, 95% CI: 1.4, 2.4** **Test for trend: B: 0.02, SE: 0.007, P=0.02**
	Maternal <u>fish</u> intake during pregnancy: Rarely/never (0 oz/wk; Ref) vs 1 meal/2wk (2.25 oz/wk) vs 1-3 meals/wk (9 oz/wk) vs 4+ meals/wk (18 oz/wk) Test for trend assesses change per oz/wk DDST: Total score (N=7116), Language (N=7135), Social (N=7127) MCDI: Vocabulary comprehension (N=7054), Social activity (N=7329)	*Higher scores on the ALSPAC adaptation of the Denver Developmental Screening Test (DDST) indicate better child performance* **ALSPAC-adapted DDST Total score at 18mo, Mean raw scores** Rarely/never: 37.2, 95% CI: 36.9, 37.6 1 meal/2wk: 37.7, 95% CI: 37.3, 38.0 1-3 meals/wk: 37.9, 95% CI: 37.6, 38.2 4+ meals/wk: 37.8, 95% CI: 37.5, 38.1 **Test for trend: B: 0.02, SE: 0.01, P=0.03** **ALSPAC-adapted DDST Language at 18mo, Mean raw scores** Rarely/never: 7.1, 95% CI: 6.9, 7.3 1 meal/2wk: 7.4, 95% CI: 7.2, 7.5 1-3 meals/wk: 7.4, 95% CI: 7.3, 7.5 4+ meals/wk: 7.4, 95% CI: 7.3, 7.6 **Test for trend: B: 0.01, SE: 0.004, P=0.004** **ALSPAC-adapted DDST Social at 18mo, Mean raw scores** Rarely/never: 8.1, 95% CI: 7.9, 8.2 1 meal/2wk: 8.1, 95% CI: 8.0, 8.2 1-3 meals/wk: 8.2, 95% CI: 8.1, 8.3 4+ meals/wk: 8.2, 95% CI: 8.0, 8.3 Test for trend: B: 0.002, SE: 0.004, P=0.5

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Daniels, 2004 **Prospective Cohort Study;** **ALSPAC; U.K.** **(Continued)**	Maternal fish intake during pregnancy: Rarely/never (0 oz/wk; Ref) vs 1 meal/2wk (2.25 oz/wk) vs 1-3 meals/wk (9 oz/wk) vs 4+ meals/wk (18 oz/wk) Test for trend assesses change per oz/wk DDST: Total score (N=7116), Language (N=7135), Social (N=7127) MCDI: Vocabulary comprehension (N=7054), Social activity (N=7329)	**ALSPAC-adapted DDST Total score at 18mo, OR for low test score (low 15 %ile)** Rarely/never (Ref) vs 1 meal/2wk: OR: 0.9, 95% CI: 0.7, 1.3 Rarely/never (Ref) vs 1-3 meals/wk: OR: 0.7, 95% CI: 0.5, 1.0 Rarely/never (Ref) vs 4+meals/wk: OR: 0.8, 95% CI: 0.6, 1.1 **Test for trend: B: -0.01, SE: 0.007, P=0.04** **ALSPAC-adapted DDST Language at 18mo, OR for low test score (low 15 %ile)** Rarely/never (Ref) vs 1 meal/2wk: OR: 0.8, 95% CI: 0.6, 1.2 **Rarely/never (Ref) vs 1-3 meals/wk: OR: 0.7, 95% CI: 0.5, 0.9** **Rarely/never (Ref) vs 4+meals/wk: OR: 0.7, 95% CI: 0.5, 0.9** **Test for trend: B: -0.02, SE: 0.007, P=0.04** **ALSPAC-adapted DDST Social at 18mo, OR for low test score (low 15 %ile)** Rarely/never (Ref) vs 1 meal/2wk: OR: 1.2, 95% CI: 0.8, 1.8 Rarely/never (Ref) vs 1-3 meals/wk: OR: 1.0, 95% CI: 0.7, 1.4 Rarely/never (Ref) vs 4+meals/wk: OR: 1.1, 95% CI: 0.7, 1.5 Test for trend: B: -0.002, SE: 0.008, P=0.7
	Maternal fish intake during pregnancy: Rarely/never (0 oz/wk; Ref) vs 1 meal/2wk (2.25 oz/wk) vs 1-3 meals/wk (9 oz/wk) vs 4+ meals/wk (18 oz/wk) Test for trend assesses change per oz/wk DDST: Total score (N=7116), Language (N=7135), Social (N=7127) MCDI: Vocabulary comprehension (N=7054), Social activity (N=7329)	**ALSPAC-adapted DDST Total score at 18mo, OR for high test score (top 15 %ile)** Rarely/never (Ref) vs 1 meal/2wk: OR: 1.0, 95% CI: 0.7, 1.5 Rarely/never (Ref) vs 1-3 meals/wk: OR: 1.4, 95% CI: 1.0, 1.9 Rarely/never (Ref) vs 4+meals/wk: OR: 1.0, 95% CI: 0.8, 1.6 Test for trend: B: 0.003, SE: 0.007, P=0.7 **ALSPAC-adapted DDST Language at 18mo, OR for high test score (top 15 %ile)** Rarely/never (Ref) vs 1 meal/2wk: OR: 1.4, 95% CI: 1.0, 1.8 Rarely/never (Ref) vs 1-3 meals/wk: OR: 1.4, 95% CI: 1.0, 1.8 Rarely/never (Ref) vs 4+meals/wk: OR: 1.3, 95% CI: 1.0, 1.8 **Test for trend: B: 0.006, SE: 0.006, P=0.03** **ALSPAC-adapted DDST Social at 18mo, OR for high test score (top 15 %ile)** Rarely/never (Ref) vs 1 meal/2wk: OR: 1.0, 95% CI: 0.8, 1.3 Rarely/never (Ref) vs 1-3 meals/wk: OR: 1.2, 95% CI: 0.9, 1.5 Rarely/never (Ref) vs 4+meals/wk: OR: 1.0, 95% CI: 0.8, 1.3 Test for trend: B: -0.001, SE: 0.008, P=0.9

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Daniels, 2004 **Prospective Cohort Study;** **ALSPAC; U.K.** **(Continued)**	Maternal fish intake during pregnancy: Rarely/never (0 oz/wk; Ref) vs 1 meal/2wk (2.25 oz/wk) vs 1-3 meals/wk (9 oz/wk) vs 4+meals/wk (18 oz/wk) N=1054 for subset with cord mercury data	Association between maternal fish intake and child cognitive development at 15mo (ALSPAC-adapted MCDI) and 18mo (ALSPAC-adapted DDST) similar with adjustment for mercury in subset with cord blood mercury. (Data NR; adjusted for cord blood mercury)
Hibbeln, 2007[7] **Prospective Cohort Study** **ALSPAC; U.K.** ***Summary:*** *Maternal fish intake >340 g/wk (vs 0 g/wk) at 32wk gestation was associated with better child development in a variety of domains including communication skills at 6 and 18mo, social development at 30 and 42mo, fine motor skills at 18 and 42mo, prosocial behavior at 7y, and verbal IQ at 8y. No other statistically significant associations between maternal fish intake and child development were detected.*	Maternal seafood intake at 32wk gestation: >340 g/wk (Ref) vs None vs 1-340 g/wk Total N~8750 at 6mo N~8230 at 18mo N~7720 at 30mo N~7600 at 42mo	*Higher scores on an ALSPAC developed scale utilizing items from the Denver Developmental Screening Test (DDST) indicate better child development* **ALSPAC-adapted DDST Gross motor skills at 6mo, OR for sub-optimum outcome (low 25 %ile)** >340 (Ref) vs 0 g/wk: OR: 1.10, 95% CI: 0.90, 1.34 >340 (Ref) vs 1-340 g/wk: OR: 1.06, 95% CI: 0.92, 1.21 P trend: 0.33 **ALSPAC-adapted DDST Fine motor skills at 6mo, OR for sub-optimum outcome (low 25 %ile)** >340 (Ref) vs 0 g/wk: OR: 1.01, 95% CI: 0.83, 1.23 >340 (Ref) vs 1-340 g/wk: OR: 1.12, 95% CI: 0.99, 1.28 P trend: 0.52 **ALSPAC-adapted DDST Social development at 6mo, OR for sub-optimum outcome (low 25 %ile)** >340 (Ref) vs 0 g/wk: OR: 1.15, 95% CI: 0.95, 1.40 >340 (Ref) vs 1-340 g/wk: OR: 1.01, 95% CI: 0.89, 1.16 P trend: 0.22 **ALSPAC-adapted DDST Communication at 6mo, OR for sub-optimum outcome (low 15 %ile)** **>340 (Ref) vs 0 g/wk: OR: 1.30, 95% CI: 1.04, 1.63** >340 (Ref) vs 1-340 g/wk: OR: 1.15, 95% CI: 0.98, 1.35 **P trend: 0.018**

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Hibbeln, 2007 **Prospective Cohort Study** **ALSPAC; U.K.** **(Continued)**	Maternal <u>seafood</u> intake at 32wk gestation: >340 g/wk (Ref) vs None vs 1-340 g/wk Total N~8750 at 6mo N~8230 at 18mo N~7720 at 30mo N~7600 at 42mo	**ALSPAC-adapted DDST Gross motor skills at 18mo, OR for sub-optimum outcome (low 25 %ile)** >340 (Ref) vs 0 g/wk: OR: 1.02, 95% CI: 0.85, 1.22 >340 (Ref) vs 1-340 g/wk: OR: 1.01, 95% CI: 0.89, 1.13 P trend: 0.84 **ALSPAC-adapted DDST Fine motor skills at 18mo, OR for sub-optimum outcome (low 25 %ile)** **>340 (Ref) vs 0 g/wk: OR: 1.25, 95% CI: 1.04, 1.51** >340 (Ref) vs 1-340 g/wk: OR: 1.09, 95% CI: 0.96, 1.23 **P trend: 0.02** **ALSPAC-adapted DDST Social development at 18mo, OR for sub-optimum outcome (low 25 %ile)** >340 (Ref) vs 0 g/wk: OR: 1.01, 95% CI: 0.83, 1.24 >340 (Ref) vs 1-340 g/wk: OR: 1.01, 95% CI: 0.88, 1.15 P trend: 0.89 **ALSPAC-adapted DDST Communication at 18mo, OR for sub-optimum outcome (low 15 %ile)** **>340 (Ref) vs 0 g/wk: OR: 1.26, 95% CI: 1.03, 1.53** >340 (Ref) vs 1-340 g/wk: OR: 1.02, 95% CI: 0.90, 1.17 **P trend: 0.048**
	Maternal <u>seafood</u> intake at 32wk gestation: >340 g/wk (Ref) vs None vs 1-340 g/wk Total N~8750 at 6mo N~8230 at 18mo N~7720 at 30mo N~7600 at 42mo	**ALSPAC-adapted DDST Gross motor skills at 30mo, OR for sub-optimum outcome (low 25 %ile)** >340 (Ref) vs 0 g/wk: OR: 0.97, 95% CI: 0.80, 1.18 >340 (Ref) vs 1-340 g/wk: OR: 1.03, 95% CI: 0.90, 1.17 P trend: 0.94 **ALSPAC-adapted DDST Fine motor skills at 30mo, OR for sub-optimum outcome (low 25 %ile)** >340 (Ref) vs 0 g/wk: OR: 1.04, 95% CI: 0.85, 1.27 >340 (Ref) vs 1-340 g/wk: OR: 1.04, 95% CI: 0.91, 1.19 P trend: 0.62 **ALSPAC-adapted DDST Social development at 30mo, OR for sub-optimum outcome (low 25 %ile)** **>340 (Ref) vs 0 g/wk: OR: 1.24, 95% CI: 1.01, 1.53** >340 (Ref) vs 1-340 g/wk: OR: 1.12, 95% CI: 0.98, 1.29 **P trend: 0.03**

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Hibbeln, 2007 **Prospective Cohort Study** **ALSPAC; U.K.** **(Continued)**		**ALSPAC-adapted DDST Gross motor skills at 42mo, OR for sub-optimum outcome (low 25 %ile)** >340 (Ref) vs 0 g/wk: OR: 0.96, 95% CI: 0.78, 1.18 >340 (Ref) vs 1-340 g/wk: OR: 0.99, 95% CI: 0.87, 1.13 P trend: 0.72 **ALSPAC-adapted DDST Fine motor skills at 42mo, OR for sub-optimum outcome (low 25 %ile)** **>340 (Ref) vs 0 g/wk: OR: 1.35, 95% CI: 1.09, 1.66** >340 (Ref) vs 1-340 g/wk: OR: 1.14, 95% CI: 0.98, 1.31 **P trend: 0.005** **ALSPAC-adapted DDST Social development at 42mo, OR for sub-optimum outcome (low 25 %ile)** >340 (Ref) vs 0 g/wk: OR: 1.21, 95% CI: 0.98, 1.50 **>340 (Ref) vs 1-340 g/wk: OR: 1.17, 95% CI: 1.01, 1.35** **P trend: 0.03**

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Hibbeln, 2007 **Prospective Cohort Study** **ALSPAC; U.K.** **(Continued)**	Maternal seafood intake at 32wk gestation: >340 g/wk (Ref) vs None vs 1-340 g/wk N~6580 at 7y	*Lower scores on the Strengths and Difficulties Questionnaire (SDQ) total score and all subscales except prosocial indicate better child behavior* **SDQ Total score at 7y, OR for sub-optimum behavioral outcomes (highest ~10%)** >340 (Ref) vs 0 g/wk: OR: 1.17, 95% CI: 0.86, 1.60 >340 (Ref) vs 1-340 g/wk: OR: 0.98, 95% CI: 0.79, 1.22 P trend: 0.38 **Prosocial at 7y, OR for sub-optimum behavioral outcomes (lowest ~10%)** **>340 (Ref) vs 0 g/wk: OR: 1.44, 95% CI: 1.05, 1.97** >340 (Ref) vs 1-340 g/wk: OR: 1.16, 95% CI: 0.93, 1.44 **P trend: 0.02** **Hyperactivity at 7y, OR for sub-optimum behavioral outcomes (highest ~10%)** >340 (Ref) vs 0 g/wk: OR: 1.13, 95% CI: 0.84, 1.53 >340 (Ref) vs 1-340 g/wk: OR: 0.91, 95% CI: 0.73, 1.12 P trend: 0.63 **Emotional at 7y, OR for sub-optimum behavioral outcomes (highest ~10%)** >340 (Ref) vs 0 g/wk: OR: 1.09, 95% CI: 0.83, 1.44 >340 (Ref) vs 1-340 g/wk: OR: 0.96, 95% CI: 0.80, 1.17 P trend: 0.68 **Conduct at 7y, OR for sub-optimum behavioral outcomes (highest ~10%)** >340 (Ref) vs 0 g/wk: OR: 1.21, 95% CI: 0.89, 1.64 >340 (Ref) vs 1-340 g/wk: OR: 1.01, 95% CI: 0.81, 1.25 P trend: 0.29 **Peer problems at 7y, OR for sub-optimum behavioral outcomes (highest ~10%)** >340 (Ref) vs 0 g/wk: OR: 1.25, 95% CI: 0.96, 1.62 >340 (Ref) vs 1-340 g/wk: OR: 0.97, 95% CI: 0.80, 1.16 P trend: 0.18

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Hibbeln, 2007 **Prospective Cohort Study** **ALSPAC; U.K.** **(Continued)**	Maternal <u>seafood</u> intake at 32wk gestation: >340 g/wk (Ref) vs None vs 1-340 g/wk N~5150 at 8y	*Higher scores on the Wechsler Intelligence Scale for Children (WISC-III) full scale, verbal, and performance IQ indicate better child cognitive performance* **WISC-III Full Scale IQ at 8y, OR for lower score (<25th%ile)** >340 (Ref) vs 0 g/wk: OR: 1.29, 95% CI: 0.99, 1.69 >340 (Ref) vs 1-340 g/wk: OR: 1.19, 95% CI: 0.99, 1.42 **P trend: 0.039** **WISC-III Verbal IQ at 8y, OR for lower score (<25th %ile)** **>340 (Ref) vs 0 g/wk: OR: 1.48, 95% CI: 1.16, 1.90** >340 (Ref) vs 1-340 g/wk: OR: 1.09, 95% CI: 0.92, 1.29 **P trend: 0.004** **>340 (Ref) vs 0 g/wk: OR: 1.67, 95% CI: 1.28, 2.13 (adjusted for 14 specific nutrients)** **>340 (Ref) vs 0 g/wk: OR: 1.39, 95% CI: 1.04, 1.86 (adjusted for paternal seafood intake)** **WISC-III Performance IQ at 8y, OR for lower score (<25th %ile)** >340(Ref) vs 0 g/wk: OR: 0.98, 95% CI: 0.76, 1.27 >340 (Ref) vs 1-340 g/wk: OR: 0.99, 95% CI: 0.84, 1.18 P trend: 0.90

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Mesirow, 2017[14] **Prospective Cohort Study** **ALSPAC; U.K.** ***Summary:*** *Children with early-onset persistent conduct problems (EOP) whose mothers ate <2 svg/wk of fish during pregnancy had greater emotional difficulties at 12-13y compared to children whose mothers ate ≥2 svg/wk of fish. No additional associations between maternal fish intake and child emotional difficulties or hyperactivity at 4-10y or 12-13y were detected for either children with EOP or children with low conduct problems.*	Maternal fish intake during pregnancy by conduct problem trajectory (Early-onset persistent conduct problems, EOP; Low conduct problems, Low CP): <2 svg/wk vs ≥2 svg/wk N=5493 (N by intake group NR)	*Lower scores on the Strengths and Difficulties Questionnaire (SDQ) subscales for emotional difficulties and hyperactivity indicate less impairment* **SDQ Emotional Difficulties at 4-10y, Group differences** <2 vs ≥2 svg/wk: F: 0.44, Effect size: 0.04, P>0.05 Interaction of fish intake by conduct problem trajectory: F: 0.14, P>0.05 EOP, <2 vs ≥2 svg/wk: Mean: 0.58, SE=0.04 vs Mean: 0.54, SE=0.06, Effect size: 0.03 Low CP, <2 vs ≥2 svg/wk: Mean: -0.16, SE=0.02 vs Mean: -0.17, SE=0.02, Effect size: 0.01 **SDQ Emotional Difficulties at 12-13y, Group differences** **<2 vs ≥2 svg/wk: F: 8.17, Effect size: 0.07, P<0.01** **Interaction of fish intake by conduct problem trajectory: F: 4.94, Effect size: 0.001, P<0.05** **EOP, <2 vs ≥2 svg/wk: Mean: 0.62, SE=0.04 vs Mean: 0.44, SE=0.06, Effect size: 0.16** **Low CP, <2 vs ≥2 svg/wk: Mean: -0.16, SE=0.02 vs Mean: -0.19, SE=0.02, Effect size: 0.03** **SDQ Hyperactivity at 4-10y, Group differences** <2 vs ≥2 svg/wk: F: 1.01, Effect size: 0.06, P>0.05 Interaction of fish intake by conduct problem trajectory: F: 0.82, P>0.05 EOP, <2 vs ≥2 svg/wk: Mean: 0.87, SE=0.04 vs Mean: 0.80, SE=0.06, Effect size: 0.10 Low CP, <2 vs ≥2 svg/wk: Mean: -0.29, SE=0.02 vs Mean: -0.29, SE=0.02, Effect size: 0.01 **SDQ Hyperactivity at 12-13y, Group differences** <2 vs ≥2 svg/wk: F: 0.14, Effect size: 0.06 P>0.05 Interaction of fish intake by conduct problem trajectory: F: 0.00, P>0.05 EOP, <2 vs ≥2 svg/wk: Mean: 0.90, SE=0.04 vs Mean: 0.88, SE=0.06, Effect size: 0.03 Low CP, <2 vs ≥2 svg/wk: Mean: -0.24, SE=0.02 vs Mean: -0.26, SE=0.02, Effect size: 0.03

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Mesirow, 2017 **Prospective Cohort Study** **ALSPAC; U.K.** **(Continued)**	Maternal fish intake during pregnancy modeled continuously (N=5348)	*EOP indicates severe conduct problem children and low CP indicates typically developing children in the Strengths and Difficulties Questionnaire (SDQ).* **Mean weekly fish intake at pregnancy and EOP and Low CP at 4-13y, Group differences** Boys: EOP vs Low CP: Mean=1.86, SE=0.09 vs Mean=2.09, SE=0.03 Girls: EOP vs Low CP: Mean=1.79, SE=0.10 vs Mean=2.06, SE=0.03 **Conduct problem trajectory: F: 11.49, P=0.001** Conduct problem trajectory*sex: F: 0.12, P=0.73
Danish National Birth Cohort (DNBC)		
Oken, 2008b[16] **Prospective Cohort Study** **DNBC; Denmark** ***Summary:*** *Higher prenatal fish intake associated with better milestone attainment at both 6mo and 18mo. The association did not vary by breastfeeding duration.*	Maternal fish intake at 25wk gestation and the previous mo in quintiles: Q1, Median=5.9 g/d (Ref, N=5744) vs Q2, Median=14.5 g/d (N=5873) vs Q3, Median=22.2 g/d (N=5913) vs Q4, Median=32.2 g/d (N=5823) vs Q5, Median=50.8 g/d (N=5605)	*Higher scores on the total development scale or motor development or social or cognitive development subscales indicate better attainment of developmental milestones at 6mo* **Total Development Scale at 6mo** Q1 (Ref) vs Q2: OR: 0.99, 95% CI: 0.92, 1.05, P=NR Q1 (Ref) vs Q3: OR: 1.05, 95% CI: 0.99, 1.13, P=NR **Q1 (Ref) vs Q4: OR: 1.09, 95% CI: 1.02, 1.17, P=NR** **Q1 (Ref) vs Q5: OR: 1.25, 95% CI: 1.17, 1.34, P=NR** **Motor Development Subscale at 6mo** Q1 (Ref) vs Q2: OR: 0.98, 95% CI: 0.92, 1.05, P=NR Q1 (Ref) vs Q3: OR: 1.03, 95% CI: 0.97, 1.11, P=NR Q1 (Ref) vs Q4: OR: 1.05, 95% CI: 0.98, 1.12, P=NR **Q1 (Ref) vs Q5: OR: 1.17, 95% CI: 1.09, 1.25, P=NR** **Social or Cognitive Development Subscale at 6mo** Q1 (Ref) vs Q2: OR: 1.0, 95% CI: 0.93, 1.07, P=NR Q1 (Ref) vs Q3: OR: 1.07, 95% CI: 0.99, 1.15, P=NR **Q1 (Ref) vs Q4: OR: 1.18, 95% CI: 1.09, 1.27, P=NR** **Q1 (Ref) vs Q5: OR: 1.33, 95% CI: 1.23, 1.44, P=NR**

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Oken, 2008b **Prospective Cohort Study** **DNBC; Denmark** **(Continued)**	Maternal <u>fish</u> intake (svg/wk) at 25wk gestation and the previous mo modeled continuously (N=25446)	*Higher scores on the total development scale or motor development or social or cognitive development subscales indicate better attainment of developmental milestones at 18mo* **Total Development Scale at 18mo** **OR: 1.49, 95% CI: 1.33, 1.66, P=NR**
	Maternal <u>fish</u> intake at 25wk gestation and the previous mo in quintiles: Q1, Median=5.9 g/d (Ref, N=5038) vs Q2, Median=14.4 g/d (N=5143) vs Q3, Median=22.2 g/d (N=5117) vs Q4, Median=32.3 g/d (N=5152) vs Q5, Median=50.7 g/d (N=4996)	**Total Development Scale at 18mo** Q1 (Ref) vs Q2: OR: 0.99, 95% CI: 0.93, 1.07, P=NR **Q1 (Ref) vs Q3: OR: 1.09, 95% CI: 1.01, 1.17, P=NR** **Q1 (Ref) vs Q4: OR: 1.14, 95% CI: 1.06, 1.22, P=NR** **Q1 (Ref) vs Q5: OR: 1.29, 95% CI: 1.20, 1.38, P=NR** **Motor Development Subscale at 18mo** Q1 (Ref) vs Q2: OR: 1.00, 95% CI: 0.93, 1.07, P=NR Q1 (Ref) vs Q3: OR: 1.08, 95% CI: 1.00, 1.16, P=NR **Q1 (Ref) vs Q4: OR: 1.11, 95% CI: 1.03, 1.19, P=NR** **Q1 (Ref) vs Q5: OR: 1.24, 95% CI: 1.15, 1.33, P=NR** **Social or Cognitive Development Subscale at 18mo** Q1 (Ref) vs Q2: OR: 1.00, 95% CI: 0.94, 1.08, P=NR **Q1 (Ref) vs Q3: OR: 1.11, 95% CI: 1.04, 1.19, P=NR** **Q1 (Ref) vs Q4: OR: 1.15, 95% CI: 1.07, 1.24, P=NR** **Q1 (Ref) vs Q5: OR: 1.28, 95% CI: 1.19, 1.37, P=NR**
	Maternal <u>fish</u> intake at 25wk gestation and the previous mo: 0 svg/wk (0 g/wk) (Ref, 11.0%) vs 1-2 svg/wk (1-340 g/wk) (86.3%) vs ≥3 svg/wk (>340 g/wk) (2.8%)	**Total Development Scale at 18mo** 0 g/wk (Ref) vs 1-340 g/wk: OR: 0.98, 95% CI: 0.85, 1.12, P=NR **0 g/wk (Ref) vs >340 g/wk: OR: 1.20, 95% CI: 1.04, 1.40, P=NR**
	Maternal <u>fish</u> intake at 25wk gestation and the previous mo in quintiles: Q1, Median=5.9 g/d (Ref) vs Q5, Median=50.7 g/d <u>Subsample: breastfed >6mo (61.4%)</u>	**Total Development Scale at 18mo** **Q1 (Ref) vs Q5: OR: 1.34, 95% CI: 1.23, 1.48, P=NR**

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Oken, 2008b **Prospective Cohort Study** **DNBC; Denmark** **(Continued)**	Maternal <u>fish</u> intake at 25wk gestation and the previous mo in quintiles: Q1, Median=5.9 g/d (Ref) vs Q5, Median=50.7 g/d <u>Subsample: breastfed up to 6mo (38.6%)</u>	**Total Development Scale at 18mo** **Q1 (Ref) vs Q5: OR: 1.23, 95% CI: 1.10, 1.38, P=NR**
Generation R Study		
Steenweg-de Graaff, 2016[21] **Prospective Cohort Study** **Generation R Study; Netherlands** ***Summary:*** *Maternal fish intake during pregnancy was not associated with nonverbal IQ at 6y.*	Maternal <u>fish</u> intake (per SD) in early pregnancy modeled continuously (N=3162) Per 1 SD increase = 13.6 g of fish intake/d.	*Higher scores on the Snijders-Oomen Niet-verbale Intelligentietest–Revisie (SON-R) indicate better child non-verbal IQ* **SON-R at 6y** B: 0.19, 95% CI: -0.28, 0.67, P=0.43
	Maternal <u>fish</u> intake in early pregnancy: No use (Ref, N=319) Vs Use (N=3483)	**SON-R at 6y** No use (Ref) vs Use: B: 1.45, 95% CI: -0.33, 3.22, P=0.11

Article	Exposure	Outcome and Results (statistically significant results are bolded)
HOME Study		
Xu, 2016[25] **Prospective Cohort Study** **HOME Study; U.S.** ***Summary:*** *Higher fish consumption during pregnancy was associated with higher asymmetric reflexes for girls (not adjusting for mercury exposure), and less need for special handling (adjusting for maternal mercury exposure). All other tested associations between fish consumption and child neurobehavior were not statistically significant.*	Maternal fish intake during entire pregnancy modeled continuously (N=344 for Maternal whole blood total Hg, N=270 for Cord whole blood total Hg)) Male (N=162) Female (N=182)	*Higher scores on the NICU Network Neurobehavioral Scale (NNNS) subscales indicate infants exhibit greater amounts of that quality (either positive or negative)* **NNNS Attention at 5wk** B: 0.003, SE: 0.005, P=0.56 (adjusted for maternal total Hg) B: 0.004, SE: 0.005, P=0.48 (adjusted for cord total Hg) **NNNS Need for Special Handling at 5wk** **B: -0.0027, SE: 0.0009, P=0.002** **B: -0.003, SE: 0.001, P=0.01 (adjusted for maternal total Hg)** B: -0.002, SE: 0.001, P=0.07 (adjusted for cord total Hg) **NNNS Asymmetry in males at 5wk** B: 0.003, SE: 0.005, P=0.55 (adjusted for maternal total Hg) B: -0.002, SE: 0.006, P=0.73 (adjusted for cord total Hg) **NNNS Asymmetry in females at 5wk** **B: 0.007, SE: 0.003, P=0.02** B: 0.005, SE: 0.004, P=0.15 (adjusted for maternal total Hg) B: 0.008, SE: 0.004, P=0.09 (adjusted for maternal total Hg)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Mount Sinai Children's Environmental Health Study		
Furlong, 2018[4] **Prospective Cohort Study** **Mount Sinai Children's Environmental Health Study; U.S.** ***Summary:*** *Maternal intake of canned fish during pregnancy was associated with higher perceptual reasoning factor scores in children 4-9y. No associations between maternal canned fish intake during pregnancy and other cognitive-behavioral factor scores were detected.*	Maternal canned fish intake during pregnancy: <1 time/wk (Ref) vs ≥1 time/wk (Analytic N=162, N by intake group NR)	*Higher scores for each factor indicate better neurodevelopmental outcomes. (Factors based on results from the BASC, BRIEF, WPPSI-III, and/or WISC-IV administered to children between 4 and 9y)* **Impulsivity and Externalizing Factor, Group differences** <1 (Ref) vs ≥1x/wk: B: 0.04, 95% CI: -0.45, 0.53, P=NR **BRIEF Executive Functioning Factor, Group differences** <1 (Ref) vs ≥1x/wk: B: -0.18, 95% CI: -0.69, 0.33, P=NR **Internalizing Factor, Group differences** <1 (Ref) vs ≥1x/wk: B: 0.11, 95% CI: -0.39, 0.61, P=NR **Perceptual Reasoning Factor, Group differences** **<1 (Ref) vs ≥1x/wk: B: 0.50, 95% CI: 0.03, 0.97, P=NR** **BASC Adaptability Factor, Group differences** <1 (Ref) vs ≥1x/wk: B: 0.28, 95% CI: -0.20, 0.77, P=NR **WPPSI-III/-IV Processing Speed Factor, Group differences** <1 (Ref) vs ≥1x/wk: B: -0.17, 95% CI: -0.66, 0.33, P=NR **WPPSI-III/-IV Verbal Intelligence Factor, Group differences** <1 (Ref) vs ≥1x/wk: B: -0.09, 95% CI: -0.51, 0.34, P=NR
Norwegian Mother and Child Cohort Study (MoBa)		
Vejrup, 2018[23] **Prospective Cohort Study** **MoBa; Norway** ***Summary:*** *Maternal seafood intake during pregnancy was positively associated with child language and communication skills at 5y*	Maternal seafood intake ≤22wk gestation in g/wk, modeled continuously (N=38,297)	*Lower scores on the Ages and Stages Questionnaire (ASQ) communication scale and its subscales indicate less communication/language impairment* **ASQ Standardized Sum Score at 5y** Increasing maternal seafood intake associated with lower scores on the ASQ (data NR)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Vejrup, 2018 **Prospective Cohort Study** **MoBa; Norway** **(Continued)**	Maternal <u>seafood</u> intake ≤22wk gestation in g/wk, modeled continuously (N=38,297)	*Lower scores on the Twenty Statements about Language-Related Difficulties List (Language 20) and its subscales indicate less communication/language impairment* **Language 20 Standardized Sum Score at 5y** Increasing maternal seafood intake associated with lower scores on the Language 20 (data NR)
		Lower scores on the Speech and Language Assessment Scale (SLAS) and its subscales indicate less communication/language impairment **SLAS Standardized Sum Score at 5y** Increasing maternal seafood intake associated with lower scores on the SLAS (data NR)
	Maternal <u>seafood</u> intake <22wk gestation: 0-100 g/wk (Ref) vs 100-400 g/wk vs >400 g/wk Analytic N=38,297 (N by intake group in adjusted analyses NR)	**ASQ Standardized Sum Score at 5y** **0-100 (Ref) vs 100-400 g/wk: B: -0.03, 95% CI: -0.07, -0.01, P=NR** **0-100 (Ref) vs >400 g/wk: B: -0.06, 95% CI: -0.1, -0.01, P<0.05** **Receptive Language Subscale** 0-100 (Ref) vs 100-400 g/wk: B: -0.02, 95% CI: -0.05, 0.01, P=NR **0-100 (Ref) vs >400 g/wk: B: -0.06, 95% CI: -0.1, -0.02, P<0.05** **Expressive Language Subscale** 0-100 (Ref) vs 100-400g/wk: B: -0.03, 95% CI: -0.06, 0.001, P=NR 0-100 (Ref) vs >400 g/wk: B: -0.02, 95% CI: -0.07, 0.02, P=NR
Vejrup, 2018 **Prospective Cohort Study;** **MoBa; Norway** **(Continued)**	Maternal <u>seafood</u> intake <22wk gestation: 0-100 g/wk (Ref) vs 100-400 g/wk vs >400 g/wk Analytic N=38,297 (N by intake group in adjusted analyses NR)	**Language 20 Standardized Sum Score at 5y** 0-100 (Ref) vs 100-400 g/wk: B: -0.03, 95% CI: -0.02, 0.1, P=NR **0-100 (Ref) vs >400 g/wk: B: -0.05, 95% CI: -0.1, -0.01, P<0.05** **Semantics Subscale** 0-100 (Ref) vs 100-400g/wk: B: -0.03, 95% CI: -0.06, 0.005, P=NR **0-100 (Ref) vs >400 g/wk: B: -0.06, 95% CI: -0.1, -0.02, P<0.05** **Responsive Subscale** 0-100 (Ref) vs 100-400 g/wk: B: -0.03, 95% CI: -0.07, 0.01, P=NR **0-100 (Ref) vs >400g/wk: B: -0.04, 95% CI: -0.09, -0.002, P<0.05** **Expressive Subscale** 0-100 (Ref) vs 100-400 g/wk: B: -0.02, 95% CI: -0.05, 0.01, P=NR 0-100 (Ref) vs >400 g/wk: B: -0.03, 95% CI: -0.07, 0.009, P=NR

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Vejrup, 2018 **Prospective Cohort Study** **MoBa; Norway** **(Continued)**		**SLAS Standardized Sum Score at 5y** 0-100 (Ref) vs 100-400 g/wk: B: -0.001, 95% CI: -0.03, 0.03, P=NR **0-100 (Ref) vs >400 g/wk: B: -0.07, 95% CI: -0.1, -0.03, P<0.05** **Assertiveness Subscale** 0-100 (Ref) vs 100-400 g/wk: B: 0.01, 95% CI: -0.02, 0.04, P=NR **0-100 (Ref) vs >400 g/wk: B: -0.05, 95% CI: -0.10, -0.01, P<0.05** **Responsiveness Subscale** 0-100 (Ref) vs 100-400g/wk: B: -0.001, 95% CI: -0.03, 0.03, P=NR **0-100 (Ref) vs >400 g/wk: B: -0.07, 95% CI: -0.11, -0.03, P<0.05** **Semantics Subscale** 0-100 (Ref) vs 100-400g/wk: B: -0.006, 95% CI: -0.04, 0.02, P=NR **0-100 (Ref) vs >400 g/wk: B: -0.07, 95% CI: -0.12, -0.03, P<0.05** **Syntax Subscale** 0-100 (Ref) vs 100-400 g/wk: B: 0.001, 95% CI: -0.03, 0.03, P=NR **0-100 (Ref) vs >400 g/wk: B: -0.07, 95% CI: -0.11, -0.02, P<0.05** **Articulation Subscale** 0-100 (Ref) vs 100-400 g/wk: B: -0.01, 95% CI: -0.04, 0.02, P=NR **0-100 (Ref) vs >400 g/wk: B: -0.06, 95% CI: -0.1, -0.02, P<0.05**
	Maternal <u>seafood</u> intake <22wk gestation: 0-100 g/wk (Ref) vs 100-400 g/wk vs >400 g/wk <u>Subsample with blood mercury measurement</u>, Analytic N=2232 (N by intake group in adjusted analyses NR)	**ASQ Standardized Sum Score at 5y** 0-100 (Ref) vs 100-400 g/wk: B: 0.01, 95% CI: -0.1, 0.1, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: 0.05, 95% CI: -0.1, 0.2, P=NR (adjusted for maternal blood Hg) **Receptive Language Subscale** 0-100 (Ref) vs 100-400 g/wk: B: 0.05, 95% CI: -0.07, 0.16, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: 0.06, 95% CI: -0.14, 0.25, P=NR (adjusted for maternal blood Hg) **Expressive Language Subscale** 0-100 (Ref) vs 100-400 g/wk: B: -0.07, 95% CI: -0.19, 0.05, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: -0.02, 95% CI: -0.22, 0.18, P=NR (adjusted for maternal blood Hg)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Vejrup, 2018 **Prospective Cohort Study** **MoBa; Norway** **(Continued)**	Maternal seafood intake <22wk gestation: 0-100 g/wk (Ref) vs 100-400 g/wk vs >400 g/wk Subsample with blood mercury measurement, Analytic N=2232 (N by intake group in adjusted analyses NR)	**Language 20 Standardized Sum Score at 5y** 0-100 (Ref) vs 100-400 g/wk: B: 0.05, 95% CI: -0.1, 0.2, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: 0.03, 95% CI: -0.1, 0.2, P=NR (adjusted for maternal blood Hg) **Semantics Subscale** 0-100 (Ref) vs 100-400 g/wk: B: 0.05, 95% CI: -0.07, 0.16, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: 0.002, 95% CI: -0.16, 0.16, P=NR (adjusted for maternal blood Hg) **Responsive Subscale** 0-100 (Ref) vs 100-400 g/wk: B: 0.02, 95% CI: -0.1, 0.14, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: 0.004, 95% CI: -0.17, 0.18, P=NR (adjusted for maternal blood Hg) **Expressive Subscale** 0-100 (Ref) vs 100-400 g/wk: B: 0.07, 95% CI: -0.04, 0.17, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: 0.09, 95% CI: -0.06, 0.24, P=NR (adjusted for maternal blood Hg)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Vejrup, 2018 **Prospective Cohort Study** **MoBa; Norway** **(Continued)**		**SLAS Standardized Sum Score at 5y** 0-100 (Ref) vs 100-400 g/wk: B: -0.03, 95% CI: -0.2, 0.1, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: -0.03, 95% CI: -0.2, 0.2, P=NR (adjusted for maternal blood Hg) **Assertiveness Subscale** 0-100 (Ref) vs 100-400 g/wk: B: -0.001, 95% CI: -0.12, 0.12, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: 0.003, 95% CI: -0.18, 0.18, P=NR (adjusted for maternal blood Hg) **Responsiveness Subscale** 0-100 (Ref) vs 100-400 g/wk: B: -0.03, 95% CI: -0.14, 0.09, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: -0.002, 95% CI: -0.18, 0.17, P=NR (adjusted for maternal blood Hg) **Semantics Subscale** 0-100 (Ref) vs 100-400 g/wk: B: -0.04, 95% CI: -0.16, 0.08, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: -0.06, 95% CI: -0.25, 0.13, P=NR (adjusted for maternal blood Hg) **Syntax Subscale** 0-100 (Ref) vs 100-400 g/wk: B: -0.06, 95% CI: -0.18, 0.07, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: -0.07, 95% CI: -0.26, 0.11, P=NR (adjusted for maternal blood Hg) **Articulation Subscale** 0-100 (Ref) vs 100-400 g/wk: B: -0.03, 95% CI: -0.15, 0.09, P=NR (adjusted for maternal blood Hg) 0-100 (Ref) vs >400 g/wk: B: -0.04, 95% CI: -0.22, 0.15, P=NR (adjusted for maternal blood Hg)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Project Viva		
Oken, 2005[19] **Prospective Cohort Study** **Project Viva; U.S.** ***Summary:*** *Higher maternal fish intake was associated with better visual recognition memory performance and the benefit was greatest among mothers who consumed >2 weekly fish svg, but had mercury levels ≤ 1.2 ppm.*	Maternal 2nd trimester fish intake svg/wk modeled continuously (N=135)	*Higher VRM scores (% novelty preference) indicate greater visual recognition memory performance* **Change in VRM score at 6.5mo (% novelty preference)** **B: 2.8, 95% CI: 0.2, 5.4** **B: 4.0, 95% CI: 1.3, 6.7 (adjusted for maternal hair Hg)**
	Maternal fish intake during 2nd trimester: ≤2 svg (Ref, N=126) vs >2 svg (N=9)	**VRM score at 6.5mo, Group differences** ≤2 (Ref) >2 svg/wk: B: 12.0, 95% CI: –0.1, 24.1 (adjusted for maternal hair Hg)
Oken, 2008a[17] **Prospective Cohort Study;** **Project Viva; U.S.** ***Summary:*** *Maternal 2nd trimester seafood intake >2 svg/wk, but not ≤2 svg/wk was associated with better visual motor abilities in children at 3y. Adjustment for erythrocyte Hg strengthened the association.*	Maternal 2nd trimester seafood intake: Never (Ref, N=47) vs ≤2 svg/wk (N=254) vs >2 svg/wk (N=40)	*Higher scores on the Peabody Picture Vocabulary Test (PPVT) indicate better child receptive vocabulary.* **PPVT at 3y, Group differences** Never (Ref) vs ≤2 svg/wk: B: -2.1. 95% CI: -5.7, 1.4, P=NR Never (Ref) vs >2 svg/wk: B: 1.2. 95% CI: -3.5, 6.0, P=NR Never (Ref) vs ≤2 svg/wk: B: -1.8. 95% CI: -5.4, 1.8, P=NR (adjusted for maternal erythrocyte Hg) Never (Ref) vs >2 svg/wk: B: 2.2. 95% CI: -2.6, 7.0, P=NR (adjusted for maternal erythrocyte Hg)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Oken, 2008a **Prospective Cohort Study;** **Project Viva; U.S.** **(Continued)**	Maternal 2nd trimester <u>seafood</u> intake: Never (Ref, N=47) vs ≤2 svg/wk (N=254) vs >2 svg/wk (N=40)	*Higher scores on the Wide Range Assessment of Visual Motor Ability (WRAVMA) total standard score and its subscales indicate better visual motor development* **WRAVMA Total Standard Score at 3y, Group differences** Never (Ref) vs ≤2 svg/wk: B: 1.1, 95% CI: -2.2, 4.4, P=NR **Never (Ref) vs >2 svg/wk: B: 5.3, 95% CI: 0.9, 9.6, P=NR** Never (Ref) vs ≤2 svg/wk: B: 1.5, 95% CI: -1.8, 4.7, P=NR (adjusted for erythrocyte Hg) **Never (Ref) vs >2 svg/wk: B: 6.4, 95% CI: 2.0, 10.8, P=NR** (adjusted for erythrocyte Hg) **Visual motor subscale (drawing test) at 3y, Group differences** Never (Ref) vs ≤2 svg/wk: B: 1.2, 95% CI: -2.0, 4.4, P=NR **Never (Ref) vs >2 svg/wk: B: 6.0, 95% CI: 1.8, 10.2, P=NR** Never (Ref) vs ≤2 svg/wk: B: 1.3, 95% CI: -1.8, 4.5, P=NR (adjusted for erythrocyte Hg) **Never (Ref) vs >2 svg/wk: B: 6.4, 95% CI: 2.1, 10.7, P=NR** (adjusted for erythrocyte Hg) **Fine-motor subscale (pegboard test) at 3y, Group differences** Never (Ref) vs ≤2 svg/wk: B: -0.7, 95% CI: -3.9, 2.4, P=NR Never (Ref) vs >2 svg/wk: B: 2.9, 95% CI: -1.4, 7.1, P=NR Never (Ref) vs ≤2 svg/wk: B: -0.5, 95% CI: -3.7, 2.7, P=NR (adjusted for erythrocyte Hg) Never (Ref) vs >2 svg/wk: B: 3.5, 95% CI: -0.8, 7.8, P=NR (adjusted for erythrocyte Hg) **Visual spatial subscale (matching test) at 3y, Group differences** Never (Ref) vs ≤2 svg/wk: B: 1.8, 95% CI: -2.6, 6.3, P=NR Never (Ref) vs >2 svg/wk: B: 2.8, 95% CI: -3.1, 8.6, P=NR Never (Ref) vs ≤2 svg/wk: B: 2.3, 95% CI: -2.1, 6.7, P=NR (adjusted for erythrocyte Hg) Never (Ref) vs >2 svg/wk: B: 4.1, 95% CI: -1.8, 10.0, P=NR (adjusted for erythrocyte Hg)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Oken, 2008a **Prospective Cohort Study;** **Project Viva; U.S.** **(Continued)**	Maternal 2nd trimester <u>seafood</u> intake by maternal erythrocyte Hg (90th %ile: 9.1 ng/g): Never (Ref, N=47) vs ≤2 svg/wk + ≤90th %ile Hg (N=229) vs ≤2 svg/wk + >90th %ile Hg (N=25) vs >2 svg/wk + ≤90th %ile Hg (N=31) vs >2 svg/wk + >90th %ile Hg (N=9)	**WRAVMA Total Standard Score at 3y, Group differences** Never (Ref) vs ≤2 svg/wk: B: 1.8, 95% CI: -1.8, 5.3, P=NR (≤90th %ile Hg) Never (Ref) vs ≤2 svg/wk: B: -4.2, 95% CI: -9.6, 1.2, P=NR (>90th %ile Hg) Never (Ref) vs >2 svg/wk: B: 5.9 95% CI: 1.0, 10.9, P=NR (≤90th %ile Hg) Never (Ref) vs >2 svg/wk: B: 4.1, 95% CI: -3.4, 11.7, P=NR (>90th %ile Hg)
	Maternal 2nd trimester <u>canned tuna fish</u> intake: Never (Ref, N=130) vs ≥2 svg/wk (N=28)	**PPVT at 3y, Group differences** Never (Ref) vs ≥2 svg/wk: B: 3.7, 95% CI: -0.9, 8.3, P=NR
	Maternal 2nd trimester <u>canned tuna fish</u> intake: Never (Ref, N=130) vs ≥2 svg/wk (N=28)	**WRAVMA Total Standard Score at 3y, Group differences** **Never (Ref) vs ≥2 svg/wk: B: 5.6, 95% CI: 1.4, 9.8, P=NR**
	Maternal 2nd trimester <u>fish intake other than canned tuna</u>: Never (Ref, N=97) vs >2 svg/wk (N=11)	**PPVT at 3y, Group differences** Never (Ref) vs >2 svg/wk: B: −1.4, 95% CI: −8.9, 6.1, P=NR
		WRAVMA Total Standard Score at 3y, Group differences Never (Ref) vs >2 svg/wk: B: 6.1, 95% CI: −0.7, 12.8, P=NR
	Maternal 2nd trimester <u>fish intake other than shellfish</u>: Never (Ref, N=NR) vs >2 svg/wk (N=NR)	**PPVT at 3y, Group differences** Never (Ref) vs >2 svg/wk: B: 4.3, 95% CI: -0.5, 9.0, P=NR
		WRAVMA Total Standard Score at 3y, Group differences **Never (Ref) vs >2 svg/wk: B: 5.9, 95%, CI: 1.6, 10.3, P=NR**

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Oken, 2016[18] **Prospective Cohort Study;** **Project Viva; U.S.** ***Summary:*** *Maternal fish consumption during mid- or late-pregnancy was not associated with child cognition in mid-childhood (~6-11y).*	Maternal seafood intake during mid-pregnancy: 0 svg/wk (Ref, N=129) vs >0-<3 svg/wk (N=800) vs ≥3 svg/wk (N=139)	*Higher scores on the Kaufman Brief Intelligence Test (KBIT-II) verbal and nonverbal IQ scales indicate better child cognitive development.* **KBIT-II Verbal IQ at 6-11y, Group Differences** 0 (Ref) vs >0-<3 svg/wk: B: 0.70, 95% CI: -1.85, 3.25, P=NR 0 (Ref) vs ≥3 svg/wk: B: 0.48, 95% CI: -2.76, 3.72, P=NR **KBIT-II Nonverbal IQ at 6-11y, Group Differences** 0 (Ref) vs >0-<3 svg/wk: B: 1.85, 95% CI: -1.44, 5.13, P=NR 0 (Ref) vs ≥3 svg/wk: B: -1.32, 95% CI: -5.49, 2.85, P=NR **KBIT-II Verbal and Nonverbal IQ (Q1 [Ref] vs Q2-4) at 6-11y, OR** 0 (Ref) vs >0-<3 svg/wk: P=NS (data NR) 0 (Ref) vs ≥3 svg/wk: P=NS (data NR)
		Higher scores on the Wide Range Assessment of Memory and Learning (WRAML) Summary Score and Subtests indicate better child memory **WRAML Summary Score at 6-11y, Group Differences** **0 (Ref) vs >0-<3 svg/wk: B: -0.98, 95% CI: -1.84, -0.11, P=NR** 0 (Ref) vs ≥3 svg/wk: B: -0.99, 95% CI: -2.11, 0.13, P=NR **Design Memory Subtest at 6-11y, Group Differences** 0 (Ref) vs >0-<3 svg/wk: B: -0.50, 95% CI: -1.04, 0.04, P=NR 0 (Ref) vs ≥3 svg/wk: B: -0.67, 95% CI: -1.36, 0.03, P=NR **Picture Memory Subtest at 6-11y, Group Differences** 0 (Ref) vs >0-<3 svg/wk: B: -0.48, 95% CI: -1.08, 0.12, P=NR 0 (Ref) vs ≥3 svg/wk: B: -0.36, 95% CI: -1.13, 0.40, P=NR

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Oken, 2016 **Prospective Cohort Study;** **Project Viva; U.S.** **(Continued)**	Maternal seafood intake during mid-pregnancy: 0 svg/wk (Ref, N=129) vs >0-<3 svg/wk (N=800) vs ≥3 svg/wk (N=139)	*Higher scores on the Wide Range of Visual Motor Abilities (WRAVMA) Drawing Subtest indicate better child visual motor abilities.* **WRAVMA Drawing Subtest at 6-11y, Group Differences** 0 (Ref) vs >0-<3 svg/wk: B: 1.40, 95% CI: -1.97, 4.76, P=NR 0 (Ref) vs ≥3 svg/wk: B: -0.26, 95% CI: -4.48, 3.96, P=NR **WRAVMA Drawing Subtest at 6-11y, Odds of being in the lowest quartile** 0 (Ref) vs >0-<3 svg/wk: P=NS (Data NR) 0 (Ref) vs ≥3 svg/wk: P=NS (Data NR)
	Maternal seafood intake (svg/wk) in mid-pregnancy modeled continuously (N=1068)	**KBIT-II Verbal and Nonverbal IQ at 6-11y, Odds of being in the lowest quartile** No association between maternal seafood intake during mid-pregnancy and risk of being in the lowest quartile for Verbal and Nonverbal IQ (data NR)
		WRAML Summary Score at 6-11y, Odds of being in the lowest quartile OR: 1.05, 95% CI: 0.81, 1.37, P=NS
		WRAVMA Drawing Subtest at 6-11y, Odds of being in the lowest quartile No association between maternal seafood intake during mid-pregnancy and risk of being in the lowest quartile for the WRAVMA Drawing Subtest (data NR)
	Maternal seafood intake (svg/wk) in mid-pregnancy modeled continuously (Subsample with erythrocyte mercury, N=872)	**KBIT-II Verbal and Nonverbal IQ at 6-11y** No association between maternal seafood intake during mid-pregnancy and Verbal or Nonverbal IQ score adjusted or unadjusted for erythrocyte mercury (data NR)
		WRAML Summary Score at 6-11y No association between maternal seafood intake during mid-pregnancy and WRAML Summary Score adjusted or unadjusted for erythrocyte mercury (data NR)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Oken, 2016 **Prospective Cohort Study;** **Project Viva; U.S.** **(Continued)**	Maternal seafood intake (svg/wk) in mid-pregnancy modeled continuously (Subsample with erythrocyte mercury, N=872)	**WRAVMA Drawing Subtest at 6-11y** No association between maternal seafood intake during mid-pregnancy and WRAVMA Drawing Subtest adjusted or unadjusted for erythrocyte mercury (data NR)
	Maternal seafood intake during mid-pregnancy: Subsample with erythrocyte mercury 0 svg/wk (Ref; N~105) vs >0-<3 svg/wk (N~662) vs ≥3 svg/wk (N~105)	**KBIT-II Verbal IQ at 6-11y, Group Differences** No association between maternal seafood intake during mid-pregnancy and Verbal IQ (data NR; adjusted for erythrocyte mercury) **KBIT-II Nonverbal IQ at 6-11y, Group Differences** No association between maternal seafood intake during mid-pregnancy and Nonverbal IQ (data NR; adjusted for erythrocyte mercury)
		WRAML Summary Score at 6-11y, Group Differences No association between maternal seafood intake during mid-pregnancy and WRAML Summary Score (data NR; adjusted for erythrocyte mercury)
		WRAVMA Drawing Subtest at 6-11y, Group Differences No association between maternal seafood intake during mid-pregnancy and WRAVMA Drawing Subtest (data NR; adjusted for erythrocyte mercury)
	Maternal seafood intake (svg/wk) in mid-pregnancy modeled continuously Subsample with data from early childhood (Oken, 2008), N=278	**KBIT-II Verbal IQ at 6-11y** B: 0.81, 95% CI: -0.20, 1.83, P=NR **KBIT-II Nonverbal IQ at 6-11y** B: -0.14, 95% CI: -1.56, 1.27, P=NR
		WRAML Summary Score at 6-11y B: -0.33, 95% CI: -0.69, 0.03, P=NR
		WRAVMA Drawing Subtest at 6-11y B: 0.00, 95% CI: -1.38, 1.38, P=NR

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Oken, 2016 **Prospective Cohort Study;** **Project Viva; U.S.** **(Continued)**	Maternal <u>seafood</u> intake in mid-pregnancy: 0 svg/wk (Ref) vs >0-<3 svg/wk vs ≥3 svg/wk Subsample of children with data from early childhood (Oken, 2008; N=278; N by intake group NR)	**KBIT-II Verbal IQ at 6-11y, Group Differences** 0x/wk (Ref) vs >0-<3 svg/wk: B: 2.01, 95% CI: -2.28, 6.29, P=NR 0x/wk (Ref) vs ≥3 svg/wk: B: 4.72, 95% CI: -0.94, 10.39, P=NR **KBIT-II Nonverbal IQ at 6-11y, Group Differences** 0x/wk (Ref) vs >0-<3 svg/wk: B: 3.59, 95% CI: -2.36, 9.54, P=NR 0x/wk (Ref) vs ≥3 svg/wk: B: 0.83, 95% CI: -7.04, 8.70, P=NR
		WRAML Summary Score at 6-11y, Group Differences 0x/wk (Ref) vs >0-<3 svg/wk: B: 0.30, 95% CI: -1.24, 1.84, P=NR 0x/wk (Ref) vs ≥3 svg/wk: B: -0.09, 95% CI: -2.13, 1.95, P=NR
		WRAVMA Drawing Subtest at 6-11y, Group Differences 0 (Ref) vs >0-<3 svg/wk: B: 1.15, 95% CI: -4.69, 7.00, P=NR 0 (Ref) vs ≥3 svg/wk: B: 0.68, 95% CI: -7.05, 8.40, P=NR
	Maternal <u>seafood</u> intake in late-pregnancy: 0 svg/wk (Ref) vs >0-<3 svg/wk vs ≥3 svg/wk N=1068 (N not reported by intake group)	**KBIT-II Verbal IQ at 6-11y, Group Differences** 0 (Ref) vs >0-<3 svg/wk: B: 2.01, 95% CI: -4.81, 8.83, P=NR 0 (Ref) vs ≥3 svg/wk: B: 2.95, 95% CI: -4.12, 10.02, P=NR **KBIT-II Nonverbal IQ at 6-11y, Group Differences** 0 (Ref) vs >0-<3 svg/wk: B: 1.63, 95% CI: -7.18, 10.43, P=NR 0 (Ref) vs ≥3 svg/wk: B: 1.44, 95% CI: -7.67, 10.55, P=NR
		WRAML Summary Score at 6-11y, Group Differences 0 (Ref) vs >0-<3 svg/wk: B: 2.09, 95% CI: -0.31, 4.50, P=NR 0 (Ref) vs ≥3 svg/wk: B: 2.17, 95% CI: -0.32, 4.66, P=NR **WRAML Summary Score at 6-11y, Odds of being in the lowest quartile** **0 (Ref) vs >0-<3 svg/wk: OR: 0.24, 95% CI: 0.08, 0.75, P=NR** **0 (Ref) vs ≥3 svg/wk: OR: 0.24, 95% CI: 0.07, 0.79, P=NR**
		WRAVMA Drawing Subtest at 6-11y, Group Differences 0 (Ref) vs >0-<3 svg/wk: B: -5.42, 95% CI: -14.5, 3.64, P=NR 0 (Ref) vs ≥3 svg/wk: B: -5.65, 95% CI: -15.0, 3.72, P=NR

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Oken, 2016 **Prospective Cohort Study;** **Project Viva; U.S.** **(Continued)**	Maternal <u>seafood</u> intake (svg/wk) in late-pregnancy modeled continuously (N=1068)	**KBIT-II Verbal IQ at 6-11y** B: 0.13, 95% CI: -0.37, 0.63, P=NR **KBIT-II Nonverbal IQ at 6-11y** B: -0.20, 95% CI: -0.85, 0.44, P=NR
		WRAML Summary Score at 6-11y B: -0.05, 95% CI: -0.23, 0.12, P=NR
		WRAVMA Drawing Subtest at 6-11y B: -0.31, 95% CI: -0.98, 0.36, P=NR
Public health impact of long-term, low-level mixed element exposure in susceptible population strata (PHIME) cohort		
Valent, 2013[22] **Prospective Cohort Study;** **PHIME Italian sub-cohort;** **Italy** ***Summary:*** *Maternal seafood intake during pregnancy was not associated with child neurodevelopment at 18mo*	Maternal <u>overall seafood</u> intake (svg/wk) during pregnancy modeled continuously (N=606)	*Higher scores on the Bayley Scales of Infant Development (BSID-III) indicate better child development* **BSID-III Cognitive, Language, Motor, Social-Emotional, and Adaptive Behavior Scores at 18mo** <u>No association</u> between maternal fish intake during pregnancy and child performance on any BSID-III score (Data NR; adjusted for total Hg in maternal hair or cord blood)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Barbone, 2019[26] **Prospective Cohort Study;** **PHIME cohort;** **Croatia, Greece, Italy, Slovenia** ***Summary:*** *Maternal seafood intake during pregnancy was not associated with child neurodevelopment at 18mo*	Maternal overall seafood intake frequency (svg/wk) during pregnancy modeled continuously (N=1308) 1 svg = 150 g (5.3 oz)	*Higher scores on the Bayley Scales of Infant and Toddler Development (BSID-III) indicate better child development* **BSID-III Cognitive composite score at 18mo** Spearman correlation: -0.03, P>0.05 **BSID-III Language composite score at 18mo** Spearman correlation: -0.01, P>0.05 **Receptive communication scaled score at 18mo** Spearman correlation: -0.02, P>0.05 **Expressive communication scaled score at 18mo** Spearman correlation: 0.003, P>0.05 **BSID-III Motor composite score at 18mo** Spearman correlation: -0.02, P>0.05 **Fine motor scaled score at 18mo** Spearman correlation: -0.03, P>0.05 **Gross motor scaled score at 18mo** Spearman correlation: -0.01, P>0.05
		Mean (SD) weekly seafood intake during pregnancy by BSID-III composite or scaled score at 18mo, Group differences **BSID-III Cognitive composite score at 18mo** ≤100 (n=465) vs >100 (n=833): 2.0 (1.4) vs 1.9 (1.5), P>0.05 **BSID-III Language composite score at 18mo** ≤91 (n=346) vs >91 (n=952): 1.9 (1.5) vs 1.9 (1.5), P>0.05 **Receptive communication scaled score at 18mo** ≤9 (n=301) vs >9 (n=995): 1.9 (1.4) vs 2.0 (1.5), P>0.05 **Expressive communication scaled score at 18mo** ≤7 (n=339) vs >7 (n=958): 1.9 (1.5) vs 2.0 (1.5), P>0.05 **BSID-III Motor composite score at 18mo** ≤97 (n=390) vs >97 (n=908): 2.0 (1.5) vs 1.9 (1.5), P>0.05 **Fine motor scaled score at 18mo** ≤10 (n=375) vs >10 (n=923): 2.1 (1.5) vs 1.9 (1.5), P>0.05 **Gross motor scaled score at 18mo** ≤8 (n=298) vs >8 (n=996): 1.9 (1.3) vs 2.0 (1.6), P>0.05

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Seychelles Child Development Study		
Davidson, 2008[2] **Prospective Cohort Study; Seychelles Child Development Study; Seychelles** ***Summary:*** *Prenatal fish intake was not associated with infant/child development at 5mo, 9mo, 25mo, or 30mo of age*	Maternal fish intake (g/d) at 28wk gestation modeled continuously (N=229 to 265)	*Higher scores on the Bayley Scales of Infant Development (BSID-II) Mental Development Index (MDI) or Psychomotor Development Index (PDI) indicate better infant or child development.* **BSID-II MDI at 9mo** No association between prenatal fish intake and MDI at 9mo in models adjusted and unadjusted for prenatal MeHg exposure (Data NR) **BSID-II PDI at 9mo** No association between prenatal fish intake and MDI at 9mo in models adjusted and unadjusted for prenatal MeHg exposure (Data NR) **BSID-II MDI at 30mo** No association between prenatal fish intake and MDI at 9mo in models adjusted and unadjusted for prenatal MeHg exposure (Data NR) **BSID-II PDI at 30mo** B: 0.02, P=0.32 B: 0.02, P=0.29 (adjusted for prenatal MeHg exposure)
	Maternal fish intake (g/d) at 28wk gestation modeled continuously (N=229 to 265)	**Fagan Infant Test (FTII) at 5mo and 9mo** No association between prenatal fish intake and FTII Mean Fixation Duration and Overall Percentage Novelty Preference at 5mo or 9mo in models adjusted and unadjusted for prenatal MeHg exposure (Data NR)
		Visual Expectation Paradigm (VEXP) at 5mo and 9mo No association between prenatal fish intake and VEXP Overall Mean Reaction Time and Overall Percentage Anticipatory Saccades at 5mo or 9mo in models adjusted and unadjusted for prenatal MeHg exposure (Data NR)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Davidson, 2008 **Prospective Cohort Study** **Seychelles Child Development Study; Seychelles** **(Continued)**	Maternal <u>fish</u> intake (g/d) at 28wk gestation modeled continuously (N=229 to 265)	**A-not-B Test at 25mo** <u>No association</u> between prenatal fish intake and A-not-B Test Overall Percentage Correct Reaches and Percentage of Lose-Stay Errors at 25mo in models adjusted and unadjusted for prenatal mercury exposure (Data NR)
		Delayed Spatial Alternation (DSA) Test at 25mo <u>No association</u> between prenatal fish intake and DSA test Overall Percentage Correct Reaches and Percentage of Lose-Stay Errors at 25mo in models adjusted and unadjusted for prenatal MeHg exposure (Data NR)
Spanish Childhood and Environment Project (INMA)		
Llop, 2012[12] **Prospective Cohort Study; INMA; Spain** ***Summary:*** *Maternal seafood intake during pregnancy was not associated with child neuro-development at 14mo of age.*	Maternal <u>total seafood</u> intake (g/wk) during pregnancy modeled continuously (N=1683)	*Higher scores on the Bayley Scales of Infant Development (BSID) indicate better child neurodevelopment* **BSID Mental Scale at 14mo** B: 0.16, 95% CI: -0.12, 0.45, P=NR (adjusted for cord blood total Hg) **BSID Psychomotor Scale at 14mo** B: -0.17, 95% CI: -0.44, 0.10, P=NR (adjusted for cord blood total Hg)
Julvez, 2016[10] **Prospective Cohort Study; INMA; Spain** ***Summary:*** *Seafood consumption during the 1st trimester had a beneficial association with child neuropsychological development at 14mo and 5y. Benefits pre-dominantly seen with small fatty, large fatty, and lean fish at moderate intake levels. No adverse associations were seen at the highest intake levels. Third trimester seafood intake weakly associated with child neuro-psychological development at 5y.*	Maternal <u>total seafood</u> consumption during 1st trimester modeled continuously in 10 g/wk increments (BSID, N=1982; MSCA, N=1589)	*Higher scores on the Bayley Scales of Infant Development (BSID) Mental and Psychomotor Scales indicate better child development* **BSID Mental Scale at 14mo** B: 0.02, 95% CI: -0.00, 0.05, P>0.05 **BSID Psychomotor Scale at 14mo** B: -0.01, 95% CI: -0.03, 0.02, P>0.05

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal total seafood consumption during 1st trimester modeled continuously in 10 g/wk increments (BSID, N=1982; MSCA, N=1589)	*Higher scores on the McCarthy Scales of Children's Abilities (MSCA) general cognitive scale and its subscale indicate better child cognitive development* **MSCA General Cognitive Scale at 5y** B: 0.02, 95% CI: 0.00, 0.05, P>0.05
	Maternal total seafood consumption during 1st trimester in quintiles: Q1 (Ref, Median=195 g/wk, N=383) vs Q2 (Median=338 g/wk, N=392) vs Q3 (Median=461 g/wk, N=364) vs Q4 (Median=600 g/wk, N=386) vs Q5 (Median= 854 g/wk N=367)	**BSID Mental Scale at 14mo, Group differences** **Q1 (Ref) vs Q2: B: 2.14, 95% CI: 0.00, 4.28, P<0.05** Q1 (Ref) vs Q3: B: 1.28, 95% CI: -0.91, 3.47, P>0.05 **Q1 (Ref) vs Q4: B: 2.90, 95% CI: 0.72, 5.09, P<0.05** Q1 (Ref) vs Q5: B: 2.06, 95% CI: -0.13, 4.26, P>0.05 P trend=0.08 **BSID Psychomotor Scale at 14mo, Group differences** **Q1 (Ref) vs Q2: B: 2.42, 95% CI: 0.27, 4.57, P<0.05** Q1 (Ref) vs Q3: B: 0.51, 95% CI: -1.69, 2.71, P>0.05 Q1 (Ref) vs Q4: B: 0.07, 95% CI: -2.12, 2.27, P>0.05 Q1 (Ref) vs Q5: B: 0.92, 95% CI: -1.30, 3.13, P>0.05 P trend=0.90

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal <u>total seafood</u> consumption during 1st trimester in quintiles: Q1 (Ref, Median=195 g/wk, N=320) vs Q2 (Median=338 g/wk, N=340) vs Q3 (Median=461 g/wk, N=299) vs Q4 (Median=600 g/wk, N=323) vs Q5 (Median= 854 g/wk N=308)	**MSCA Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: 1.61, 95% CI: -0.43, 3.65, P>0.05 **Q1 (Ref) vs Q3: B: 2.13, 95% CI: 0.00, 4.26, P<0.05** **Q1 (Ref) vs Q4: B: 2.84, 95% CI: 0.74, 4.94, P<0.05** Q1 (Ref) vs Q5: B: 2.08, 95% CI: -0.04, 4.21, P>0.05 **P trend=0.049** **Verbal Subscale at 5y, Group differences** Q1 (Ref) vs Q2: B: 1.17, 95% CI: -0.98, 3.33, P>0.05 Q1 (Ref) vs Q3: B: 0.54, 95% CI: -1.70, 2.78, P>0.05 **Q1 (Ref) vs Q4: B: 2.36, 95% CI: 0.14, 4.57, P<0.05** Q1 (Ref) vs Q5: B: 1.57, 95% CI: -0.67, 3.81, P>0.05 **Perceptual-performance Subscale at 5y, Group differences** Q1 (Ref) vs Q2: B: 1.66, 95% CI: -0.43, 3.75, P>0.05 **Q1 (Ref) vs Q3: B: 2.29, 95% CI: 0.11, 4.46, P<0.05** Q1 (Ref) vs Q4: B: 1.62, 95% CI: -0.53, 3.77, P>0.05 Q1 (Ref) vs Q5: B: 1.74, 95% CI: -0.44, 3.91, P>0.05 **Memory Subscale at 5y, Group differences** Q1 (Ref) vs Q2: B: 1.91, 95% CI: -0.27, 4.10, P>0.05 Q1 (Ref) vs Q3: B: 1.50, 95% CI: -0.78, 3.78, P>0.05 **Q1 (Ref) vs Q4: B: 3.34, 95% CI: 1.09, 5.60, P<0.05** Q1 (Ref) vs Q5: B: 1.94, 95% CI: -0.34, 4.22, P>0.05 **Quantitative Subscale at 5y, Group differences** Q1 (Ref) vs Q2: B: 1.04, 95% CI: -1.12, 3.20, P>0.05 **Q1 (Ref) vs Q3: B: 3.11, 95% CI: 0.86, 5.37, P<0.05** **Q1 (Ref) vs Q4: B: 3.09, 95% CI: 0.86, 5.31, P<0.05** Q1 (Ref) vs Q5: B: 1.56, 95% CI: -0.69, 3.81, P>0.05 **Motor Subscale at 5y, Group differences** Q1 (Ref) vs Q2: B: 1.81, 95% CI: -0.36, 3.96, P>0.05 **Q1 (Ref) vs Q3: B: 2.91, 95% CI: 0.68, 5.17, P<0.05** **Q1 (Ref) vs Q4: B: 2.48, 95% CI: 0.26, 4.69, P<0.05** Q1 (Ref) vs Q5: B: 1.61, 95% CI: -0.62, 3.85, P>0.05 **Executive function Subscale at 5y, Group differences** Q1 (Ref) vs Q2: B: 1.06, 95% CI: -1.02, 3.14, P>0.05 Q1 (Ref) vs Q3: B: 1.74, 95% CI: -0.43, 3.91, P>0.05 **Q1 (Ref) vs Q4: B: 2.83, 95% CI: 0.69, 4.98, P<0.05** Q1 (Ref) vs Q5: B: 1.93, 95% CI: -0.24, 4.09, P>0.05

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal total seafood consumption during 1st trimester in quintiles: Q1 (Ref ≤340 g, Median=243 g/wk, N=592) vs Q2 (Median= 370 g/wk, N=183) vs Q3 (Median=461 g/wk, N=364) vs Q4 (Median=600 g/wk, N=386) vs Q5 (Median=854 g/wk N=367)	**BSID Mental Scale at 14mo, ref group ≤340 g, Group differences** Q1 (Ref) vs Q2: B: 2.23, 95% CI: -0.28, 4.74, P>0.05 Q1 (Ref) vs Q3: B: 0.73, 95% CI: -1.27, 4.71, P>0.05 **Q1 (Ref) vs Q4: B: 2.33, 95% CI: 0.35, 4.30, P<0.05** Q1 (Ref) vs Q5: B: 1.51, 95% CI: -0.49, 3.51, P>0.05 P trend=0.10 **BSID Psychomotor Scale at 14 mo, ref group ≤340 g, Group differences** Results similar to when quintiles composed of ~equal numbers of participants (data NR)
		MSCA General Cognitive Scale at 5y, ref group ≤340 g, Group differences Q1 (Ref) vs Q2: B: 1.81, 95% CI: -0.55, 4.17, P>0.05 Q1 (Ref) vs Q3: B: 1.75, 95% CI: -0.18, 3.69, P>0.05 **Q1 (Ref) vs Q4: B: 2.46, 95% CI: 0.56, 4.36, P<0.05** Q1 (Ref) vs Q5: B: 1.71, 95% CI: -0.23, 3.65, P>0.05 P trend=0.057
	Maternal total seafood consumption during 1st trimester modeled continuously in 10 g/wk increments (Subsample with cord blood mercury, N=1221; Subsample with long chain PUFA, N=611)	**MSCA General Cognitive Scale at 5y** B: 0.00, 95% CI: -0.03, 0.03, P>0.05 (adjusted for cord Hg) B: 0.03, 95% CI: -0.01, 0.07, P>0.05 (adjusted for cord LCPUFA)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal <u>total seafood</u> consumption during 1st trimester in quintiles: Q1 (Ref, Median=195 g/wk, N=241) vs Q2 (Median=338 g/wk, N=249) vs Q3 (Median=461 g/wk, N=240) vs Q4 (Median=600 g/wk, N=262) vs Q5 (Median 854 g/wk N=230) <u>Subsample with cord blood mercury</u> Maternal <u>total seafood</u> consumption during 1st trimester in quintiles: Q1 (Ref, Median=195 g/wk, N=131) vs Q2 (Median=338 g/wk, N=115) vs Q3 (Median=461 g/wk, N=115) vs Q4 (Median=600 g/wk, N=125) vs Q5 (Median 854 g/wk N=125) <u>Subsample with cord blood long chain PUFA</u>	**MSCA General Cognitive Scale at 5y, Group differences** (adjusted for cord blood Hg) Q1 (Ref) vs Q2: B: 0.56, 95% CI: -1.82, 2.93, P>0.05 Q1 (Ref) vs Q3: B: 1.22, 95% CI: -1.25, 3.69, P>0.05 Q1 (Ref) vs Q4: B: 1.71, 95% CI: -0.71, 4.13, P>0.05 Q1 (Ref) vs Q5: B: 0.15, 95% CI: -2.36, 2.66, P>0.05 P trend=0.80 (adjusted for cord blood LCPUFA) Q1 (Ref) vs Q2: B: -0.27, 95% CI: -3.53, 2.98, P>0.05 Q1 (Ref) vs Q3: B: 2.14 95% CI: -1.15, 5.44, P>0.05 Q1 (Ref) vs Q4: B: 2.92, 95% CI: -0.29, 6.14, P>0.05 Q1 (Ref) vs Q5: B: 1.34, 95% CI: -1.92, 4.60, P>0.05 P trend=0.19
	Maternal <u>total seafood</u> consumption during 1st trimester modeled continuously in 10 g/wk increments (N=671) Subsample: Cantabric Sea	**MSCA General Cognitive Scale at 5y** B: 0.02, 95% CI: -0.01, 0.06, P>0.05
	Maternal <u>total seafood</u> consumption during 1st trimester modeled continuously in 10 g/wk increments (N=919) Subsample: Mediterranean Sea	**MSCA General Cognitive Scale at 5y** B: 0.03, 95% CI: -0.01, 0.07, P>0.05
	Maternal <u>total seafood</u> consumption during 1st trimester in quintiles, Q1 (Ref, N=98) vs Q2 (N=128) vs Q3 (N=128) vs Q4 (N=160) vs Q5 (N=157) Subsample: Cantabric Sea	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: 0.04, 95% CI: -3.61, 3.70, P>0.05 Q1 (Ref) vs Q3: B: 1.23, 95% CI: -2.45, 4.92, P>0.05 **Q1 (Ref) vs Q4: B: 3.84, 95% CI: 0.32, 7.35, P<0.05** Q1 (Ref) vs Q5: B: 1.09, 95% CI: -2.44, 4.61, P>0.05 P trend=0.25

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal <u>total seafood</u> consumption during 1st trimester in quintiles, Q1 (Ref, N=222) vs Q2 (N=212) vs Q3 (N=171) vs Q4 (N=163) vs Q5 (N=153) Subsample: Mediterranean Sea	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: 2.30, 95% CI: -0.20, 4.79, P>0.05 **Q1 (Ref) vs Q3: B: 2.73, 95% CI: 0.07, 5.39, P<0.05** Q1 (Ref) vs Q4: B: 1.89, 95% CI: -0.82, 4.61, P>0.05 **Q1 (Ref) vs Q5: B: 3.46, 95% CI: 0.68, 6.23, P<0.05** **P trend=0.03**
	Maternal <u>large fatty fish</u> consumption during 1st trimester modeled continuously in 10 g/wk increments (BSID, N=1982; MSCA, N=1589)	**BSID Mental Scale at 14mo** B: 0.00, 95% CI: -0.07, 0.08, P>0.05 **BSID Psychomotor Scale at 14mo** B: 0.02, 95% CI: -0.06, 0.09, P>0.05
		MSCA General Cognitive Scale at 5y B: 0.06, 95% CI: -0.00, 0.13, P>0.05
	Maternal <u>large fatty fish</u> consumption during 1st trimester in quartiles: Q1 (Ref, None, N=853) vs Q2 (Median=48 g/wk, N=341) vs Q3 (Median=92 g/wk, N=345) vs Q4 (Median=238 g/wk, N=353)	**BSID Mental Scale at 14mo, Group differences** Q1 (Ref) vs Q2: B: 0.08, 95% CI: -1.84, 2.01, P>0.05 Q1 (Ref) vs Q3: B: -0.12, 95% CI: -2.06, 1.82, P>0.05 Q1 (Ref) vs Q4: B: 0.51, 95% CI: -1.43, 2.46, P>0.05 P trend=0.62 **BSID Psychomotor Scale at 14mo, Group differences** Q1 (Ref) vs Q2: B: -0.46, 95% CI: -2.39, 1.47, P>0.05 Q1 (Ref) vs Q3: B: 1.56, 95% CI: -0.38, 3.50, P>0.05 Q1 (Ref) vs Q4: B: -0.13, 95% CI: -2.07, 1.82, P>0.05 P trend=0.93
		MSCA Cognitive Scale at 5y, Group differences **Q1 (Ref) vs Q2: B: 2.26, 95% CI: 0.40, 4.11, P<0.05** **Q1 (Ref) vs Q3: B: 1.93, 95% CI: 0.09, 3.79, P<0.05** **Q1 (Ref) vs Q4: B: 2.29, 95% CI: 0.42, 4.16, P<0.05** **P trend=0.02**

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal large fatty fish consumption during 1st trimester modeled continuously in 10 g/wk increments (Subsample with cord blood mercury, N=1221; Subsample with cord blood long chain PUFA, N=611)	**MSCA General Cognitive Scale at 5y** Adjusted for cord Hg: B: 0.03, 95% CI: -0.06, 0.11, P>0.05^ Adjusted for cord LCPUFA: B: 0.04, 95% CI: -0.08, 0.16, P>0.05
	Maternal large fatty fish consumption during 1st trimester in quartiles: Q1 (Ref, None, N=535) vs Q2 (Median=48 g/wk, N=218) vs Q3 (Median=92 g/wk, N=231) vs Q4 (Median=238 g/wk, N=3237) Subsample with cord blood mercury Maternal large fatty fish consumption during 1st trimester in quartiles: Q1 (Ref, None, N=281) vs Q2 (Median=48 g/wk, N=118) vs Q3 (Median=92 g/wk, N=105) vs Q4 (Median=238 g/wk, N=107) Subsample with cord blood long chain PUFA	**MSCA General Cognitive Scale at 5y, Group differences** Adjusted for cord blood Hg Q1 (Ref) vs Q2: B: 1.53, 95% CI: -0.59, 3.66, P>0.05 Q1 (Ref) vs Q3: B: 0.53, 95% CI: -1.59, 2.66, P>0.05 Q1 (Ref) vs Q4: B: 1.31, 95% CI: -0.81, 3.44, P>0.05 P trend=0.28^ Adjusted for cord blood LCPUFA **Q1 (Ref) vs Q2: B: 3.79, 95% CI: 0.97, 6.60, P<0.05** Q1 (Ref) vs Q3: B: 2.27 95% CI: -0.73, 5.28, P>0.05 Q1 (Ref) vs Q4: B: 2.32, 95% CI: -0.68, 5.33, P>0.05 P trend=0.18
	Maternal large fatty fish consumption during 1st trimester modeled continuously in 10 g/wk increments (N=671) Subsample: Cantabric Sea	**MSCA General Cognitive Scale at 5y** B: 0.08, 95% CI: -0.02, 0.17, P>0.05
	Maternal large fatty fish consumption during 1st trimester modeled continuously in 10 g/wk increments (N=919) Subsample: Mediterranean Sea	**MSCA General Cognitive Scale at 5y** B: 0.07, 95% CI: -0.03, 0.17, P>0.05

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal large fatty fish consumption during 1st trimester in quartiles: Q1 (Ref, N=229) vs Q2 (N=114) vs Q3 (N=146) vs Q4 (N=182) Subsample: Cantabric Sea	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: -0.24, 95% CI: -3.39, 2.91, P>0.05 Q1 (Ref) vs Q3: B: 1.09, 95% CI: -1.84, 4.03, P>0.05 Q1 (Ref) vs Q4: B: 2.00, 95% CI: -0.75, 4.75, P>0.05 P trend=0.12
	Maternal large fatty fish consumption during 1st trimester in quartiles: Q1 (Ref, N=475) vs Q2 (N=171) vs Q3 (N=150) vs Q4 (N=120) Subsample: Mediterranean Sea	**MSCA General Cognitive Scale at 5y, Group differences** **Q1 (Ref) vs Q2: B: 2.81, 95% CI: 0.47, 5.15, P<0.05** Q1 (Ref) vs Q3: B: 2.08, 95% CI: -0.39, 4.54, P>0.05 Q1 (Ref) vs Q4: B: 2.22, 95% CI: -0.45, 4.88, P>0.05 P trend=0.07
	Maternal small fatty fish consumption during 1st trimester modeled continuously in 10 g/wk increments (BSID, N=1982; MSCA, N=1589)	**BSID Mental Scale at 14mo** B: 0.06, 95% CI: -0.02, 0.15, P>0.05 **BSID Psychomotor Scale at 14mo** B: 0.05, 95% CI: -0.03, 0.14, P>0.05
		MSCA General Cognitive Scale at 5y B: -0.03, 95% CI: -0.10, 0.05, P>0.05
	Maternal small fatty fish consumption during 1st trimester in quartiles: Q1 (Ref, None, N=877) vs Q2 (Median=37 g/wk, N=333) vs Q3 (Median=69 g/wk, N=338) vs Q4 (Median=147 g/wk, N=344)	**BSID Mental Scale at 14mo, Group differences** Q1 (Ref) vs Q2: B: 1.79, 95% CI: -0.22, 3.80, P>0.05 Q1 (Ref) vs Q3: B: -0.37, 95% CI: -2.29, 1.55, P>0.05 **Q1 (Ref) vs Q4: B: 2.45, 95% CI: 0.54, 4.36, P<0.05** **P trend=0.03** **BSID Psychomotor Scale at 14mo, Group differences** Q1 (Ref) vs Q2: B: -0.58, 95% CI: -2.60, 1.44, P>0.05 Q1 (Ref) vs Q3: B: -0.26, 95% CI: -2.19, 1.67, P>0.05 Q1 (Ref) vs Q4: B: 1.55, 95% CI: -0.37, 3.47, P>0.05 P trend=0.14

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal small fatty fish consumption during 1st trimester in quartiles: Q1 (Ref, None, N=736) vs Q2 (Median=37 g/wk, N=280) vs Q3 (Median=69 g/wk, N=288) vs Q4 (Median=147 g/wk, N=285)	**MSCA Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: 0.60, 95% CI: -1.33, 2.53, P>0.05 Q1 (Ref) vs Q3: B: 1.25, 95% CI: -0.59, 3.10, P>0.05 Q1 (Ref) vs Q4: B: 0.91, 95% CI: -0.93, 2.76, P>0.05 P trend=0.25
	Maternal small fatty fish consumption during 1st trimester modeled continuously in 10 g/wk increments (N=671) Subsample: Cantabric Sea	**MSCA General Cognitive Scale at 5y** B: 0.06, 95% CI: -0.06, 0.18, P>0.05
	Maternal small fatty fish consumption during 1st trimester modeled continuously in 10 g/wk increments (N=919) Subsample: Mediterranean Sea	**MSCA General Cognitive Scale at 5y** B: -0.09, 95% CI: -0.20, 0.01, P>0.05
	Maternal small fatty fish consumption during 1st trimester in quartiles: Q1 (Ref, N=337) vs Q2 (N=101) vs Q3 (N=106) vs Q4 (N=127) Subsample: Cantabric Sea	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: -1.80, 95% CI: -5.06, 1.45, P>0.05 Q1 (Ref) vs Q3: B: 0.78, 95% CI: -2.27, 3.84, P>0.05 Q1 (Ref) vs Q4: B: 1.30, 95% CI: -1.56, 4.15, P>0.05 P trend=0.32
	Maternal small fatty fish consumption during 1st trimester in quartiles, Q1 (Ref, N=399) vs Q2 (N=179) vs Q3 (N=182) vs Q4 (N=158) Subsample: Mediterranean Sea	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: 1.07, 95% CI: -1.36, 3.50, P>0.05 Q1 (Ref) vs Q3: B: 1.29, 95% CI: -1.06, 3.65, P>0.05 Q1 (Ref) vs Q4: B: 0.58, 95% CI: -1.92, 3.07, P>0.05 P trend=0.54

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal <u>lean fish</u> consumption during 1st trimester modeled continuously in 10 g/wk increments (BSID, N=1982; MSCA, N=1589)	**BSID Mental Scale at 14mo** B: 0.03, 95% CI: -0.00, 0.07, P>0.05 **BSID Psychomotor Scale at 14mo** B: -0.02, 95% CI: -0.05, 0.02, P>0.05
		MSCA General Cognitive Scale at 5y B: 0.03, 95% CI: -0.01, 0.06, P>0.05
	Maternal <u>lean fish</u> consumption during 1st trimester in quintiles: Q1 (Ref, Median=90 g/wk, N=387) vs Q2 (Median=192 g/wk, N=386) vs Q3 (Median=286 g/wk, N=380) vs Q4 (Median=382 g/wk, N=372) vs Q5 (Median=557 g/wk, N=367)	**BSID Mental Scale at 14mo, Group differences** Q1 (Ref) vs Q2: B: 0.44, 95% CI: -1.71, 2.58, P>0.05 Q1 (Ref) vs Q3: B: 2.07, 95% CI: -0.12, 4.26, P>0.05 Q1 (Ref) vs Q4: B: 1.41, 95% CI: -0.78, 3.59, P>0.05 Q1 (Ref) vs Q5: B: 1.77, 95% CI: -0.46, 3.99, P>0.05 P trend=0.10 **BSID Psychomotor Scale at 14mo, Group differences** Q1 (Ref) vs Q2: B: 1.67, 95% CI: -0.47, 3.82, P>0.05 **Q1 (Ref) vs Q3: B: 2.50, 95% CI: 0.30, 4.69, P<0.05** Q1 (Ref) vs Q4: B: -0.62, 95% CI: -2.81, 1.57, P>0.05 Q1 (Ref) vs Q5: B: 1.10, 95% CI: -1.13, 3.34, P>0.05 P trend=0.99
	Maternal <u>lean fish</u> consumption during 1st trimester in quintiles: Q1 (Ref, Median=90 g/wk, N=328) vs Q2 (Median=192 g/wk, N=325) vs Q3 (Median=286 g/wk, N=322) vs Q4 (Median=382 g/wk, N=307) vs Q5 (Median=557 g/wk, N=307)	**MSCA Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: 1.76, 95% CI: -0.29, 3.81, P>0.05 Q1 (Ref) vs Q3: B: 2.01, 95% CI: -0.08, 4.11, P>0.05 **Q1 (Ref) vs Q4: B: 2.47, 95% CI: 0.36, 4.58, P<0.05** Q1 (Ref) vs Q5: B: 1.89, 95% CI: -0.25, 4.03, P>0.05 P trend=0.11
	Maternal <u>lean fish</u> consumption during 1st trimester modeled continuously in 10 g/wk increments (<u>Subsample with cord blood mercury</u>, N=1221; <u>Subsample with cord blood long chain PUFA</u>, N=611)	**MSCA General Cognitive Scale at 5y** B: 0.00, 95% CI: -0.04, 0.05, P>0.05^ (adjusted for cord Hg) B: 0.05, 95% CI: -0.00, 0.11, P>0.05 (adjusted for cord LCPUFA)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study; INMA; Spain** **(Continued)**	Maternal <u>lean fish</u> consumption during 1st trimester in quintiles: <u>Subsample with cord blood mercury</u> Q1 (Ref, Median=90 g/wk, N=243) vs Q2 (Median=192 g/wk, N=253) vs Q3 (Median=286 g/wk, N=3238) vs Q4 (Median=382 g/wk, N=250) vs Q5 (Median=557 g/wk, N=237) <u>Subsample with cord blood long chain PUFA</u> Maternal <u>lean fish</u> consumption during 1st trimester in quintiles: Q1 (Ref, Median=90 g/wk, N=123) vs Q2 (Median=192 g/wk, N=130) vs Q3 (Median=286 g/wk, N=107) vs Q4 (Median=382 g/wk, N=131) vs Q5 (Median=557 g/wk, N=120)	**MSCA General Cognitive Scale at 5y, Group differences** Adjusted for cord blood Hg Q1 (Ref) vs Q2: B: 1.75, 95% CI: -0.60, 4.11, P>0.05 Q1 (Ref) vs Q3: B: 0.46, 95% CI: -1.99, 2.92, P>0.05 Q1 (Ref) vs Q4: B: 1.28, 95% CI: -1.15, 3.71, P>0.05 Q1 (Ref) vs Q5: B: 0.90, 95% CI: -1.60, 3.40, P>0.05 P trend=0.72 Adjusted for cord blood LCPUFA Q1 (Ref) vs Q2: B: -0.15, 95% CI: -3.34, 3.05, P<0.05 Q1 (Ref) vs Q3: B: 0.06 95% CI: -3.33, 3.45, P>0.05 Q1 (Ref) vs Q4: B: 2.82, 95% CI: -0.40, 6.05, P>0.05 Q1 (Ref) vs Q5: B: 1.82, 95% CI: -0.40, 5.12, P>0.05 P trend=0.10
	Maternal <u>lean fish</u> consumption during 1st trimester modeled continuously in 10 g/wk increments (N=671) Subsample: Cantabric Sea	**MSCA General Cognitive Scale at 5y** B: 0.00, 95% CI: -0.05, 0.06, P>0.05
	Maternal <u>lean fish</u> consumption during 1st trimester modeled continuously in 10 g/wk increments (N=919) Subsample: Mediterranean Sea	**MSCA General Cognitive Scale at 5y** **B: 0.07, 95% CI: 0.02, 0.10, P<0.05**
	Maternal <u>lean fish</u> consumption during 1st trimester in quintiles Q1 (Ref, N=82) vs Q2 (N=123) vs Q3 (N=149) vs Q4 (N=139) vs Q5 (N=178) Subsample: Cantabric Sea	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: 1.20, 95% CI: -2.70, 5.10, P>0.05 Q1 (Ref) vs Q3: B: 2.36, 95% CI: -1.42, 6.15, P>0.05 Q1 (Ref) vs Q4: B: 1.79, 95% CI: -2.05, 5.64, P>0.05 Q1 (Ref) vs Q5: B: 0.98, 95% CI: -2.70, 4.67, P>0.05 P trend=0.89

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal lean fish consumption during 1st trimester in quintiles, Q1 (Ref, N=246) vs Q2 (N=202) vs Q3 (N=173) vs Q4 (N=168) vs Q5 (N=129) Subsample: Mediterranean Sea	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: 1.42, 95% CI: -1.05, 3.90, P>0.05 Q1 (Ref) vs Q3: B: 1.19, 95% CI: -1.43, 3.82, P>0.05 **Q1 (Ref) vs Q4: B: 2.98, 95% CI: 0.36, 5.61, P<0.05** **Q1 (Ref) vs Q5: B: 3.16, 95% CI: 0.30, 6.02, P<0.05** **P trend=0.01**
	Maternal shellfish consumption during 1st trimester modeled continuously in 10 g/wk increments (BSID, N=1892; MSCA, N=1589)	**BSID Mental Scale at 14mo** B: 0.05, 95% CI: -0.06, 0.16, P>0.05 **BSID Psychomotor Scale at 14mo** B: 0.04, 95% CI: -0.07, 0.16, P>0.05
		MSCA General Cognitive Scale at 5y B: -0.02, 95% CI: -0.13, 0.09, P>0.05
	Maternal shellfish consumption during 1st trimester in quintiles: Q1 (Ref, None, N=373) vs Q2 (Median=27 g/wk, N=370) vs Q3 (Median=49 g/wk, N=384) vs Q4 (Median=76 g/wk, N=394) vs Q5 (Median=139 g/wk, N=371)	**BSID Mental Scale at 14mo, Group differences** Q1 (Ref) vs Q2: B: 0.80, 95% CI: -1.41, 3.01, P>0.05 Q1 (Ref) vs Q3: B: 1.86, 95% CI: -0.30, 4.03, P>0.05 Q1 (Ref) vs Q4: B: 1.45, 95% CI: -0.70, 3.61, P>0.05 Q1 (Ref) vs Q5: B: 1.52, 95% CI: -0.72, 3.75, P>0.05 P trend=0.21 **BSID Psychomotor Scale at 14mo, Group differences** Q1 (Ref) vs Q2: B: -1.34, 95% CI: -3.56, 0.88, P>0.05 Q1 (Ref) vs Q3: B: -0.75, 95% CI: -2.93, 1.42, P>0.05 Q1 (Ref) vs Q4: B: 0.25, 95% CI: -1.92, 2.41, P>0.05 Q1 (Ref) vs Q5: B: 1.02, 95% CI: -1.23, 3.26, P>0.05 P trend=0.16
		MSCA Cognitive Scale at 5y, Group differences Q1 (Ref) vs Q2: B: -0.12, 95% CI: -2.26, 2.02, P>0.05 Q1 (Ref) vs Q3: B: 0.81, 95% CI: -1.27, 2.90, P>0.05 Q1 (Ref) vs Q4: B: 0.79, 95% CI: -2.29, 2.88, P>0.05 Q1 (Ref) vs Q5: B: -0.94, 95% CI: -3.10, 1.22, P>0.05 P trend=0.44

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal <u>shellfish</u> consumption during 1st trimester modeled continuously in 10 g/wk increments (N=671) Subsample: Cantabric Sea	**MSCA General Cognitive Scale at 5y** B: 0.06, 95% CI: -0.11, 0.23, P>0.05
	Maternal <u>shellfish</u> consumption during 1st trimester modeled continuously in 10 g/wk increments (N=919) Subsample: Mediterranean Sea	**MSCA General Cognitive Scale at 5y** B: -0.06, 95% CI: -0.21, 0.09, P>0.05
	Maternal <u>shellfish</u> consumption during 1st trimester in quintiles, Q1 (Ref, N=162) vs Q2 (N=188) vs Q3 (N=192) vs Q4 (N=192) vs Q5 (N=184) Subsample: Mediterranean Sea	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: -0.56, 95% CI: -3.39, 2.26, P>0.05 Q1 (Ref) vs Q3: B: -0.58, 95% CI: -3.37, 2.21, P>0.05 Q1 (Ref) vs Q4: B: -1.20, 95% CI: -1.20, 1.60, P>0.05 Q1 (Ref) vs Q5: B: -2.63, 95% CI: -2.63, 0.26, P>0.05 P trend=0.06
	Maternal <u>shellfish</u> consumption during 1st trimester in quintiles, Q1 (Ref, N=145) vs Q2 (N=119) vs Q3 (N=139) vs Q4 (N=140) vs Q5 (N=128) Subsample: Cantabric Sea	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: -0.66, 95% CI: -4.05, 2.73, P>0.05 Q1 (Ref) vs Q3: B: 2.40, 95% CI: -0.85, 5.64, P>0.05 Q1 (Ref) vs Q4: B: 3.09, 95% CI: -0.13, 6.31, P>0.05 Q1 (Ref) vs Q5: B: 1.92, 95% CI: -1.43, 5.28, P>0.05 P trend=0.12
	Maternal <u>total seafood</u> consumption during 3rd trimester modeled continuously in 10 g/wk increments (N=1567)	**MSCA General Cognitive Scale at 5y** B: 0.01, 95% CI: -0.01, 0.04, P>0.05 **Perceptual-performance Subscale at 5y** B: 0.02, 95% CI: -0.00, 0.04, P>0.05

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal <u>total seafood</u> consumption during 3rd trimester in quintiles: Q1 (Ref, Median=196 g/wk, N=324) vs Q2 (Median=337 g/wk, N=320) vs Q3 (Median=455 g/wk, N=298) vs Q4 (Median=585 g/wk, N=316) vs Q5 (Median=828 g/wk N=309)	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: -1.41, 95% CI: -3.47, 0.66, P>0.05 Q1 (Ref) vs Q3: B: -0.68, 95% CI: -2.81, 1.45, P>0.05 Q1 (Ref) vs Q4: B: -0.29, 95% CI: -2.40, 1.83, P>0.05 Q1 (Ref) vs Q5: B: 0.73, 95% CI: -1.39, 2.86, P>0.05 P trend=0.23 **Perceptual-performance Subscale at 5y, Group differences** Q1 (Ref) vs Q2: B: -0.67, 95% CI: -2.78, 1.43, P>0.05 Q1 (Ref) vs Q3: B: -0.17, 95% CI: -2.34, 2.00, P>0.05 Q1 (Ref) vs Q4: B: 2.09, 95% CI: -0.06, 4.24, P>0.05 Q1 (Ref) vs Q5: B: 1.34, 95% CI: -0.81, 3.51, P>0.05 **P trend=0.04**
	Maternal <u>large fatty fish</u> consumption during 3rd trimester modeled continuously in 10 g/wk increments (N=1567)	**MSCA General Cognitive Scale at 5y** **B: 0.07, 95% CI: 0.00, 0.14, P<0.05** **Perceptual-performance Subscale at 5y** **B: 0.07, 95% CI: 0.00, 0.14, P<0.05**
	Maternal <u>large fatty fish</u> consumption during 3rd trimester in quartiles: Q1 (Ref, None, N=652) vs Q2 (Median=45 g/wk, N=290) vs Q3 (Median=93 g/wk, N=313) vs Q4 (Median=253 g/wk, N=310)	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: 1.29, 95% CI: -0.62, 3.19, P>0.05 Q1 (Ref) vs Q3: B: 1.49, 95% CI: -0.38, 3.36, P>0.05 Q1 (Ref) vs Q4: B: 1.89, 95% CI: -0.04, 3.82, P>0.05 P trend=0.06 **Perceptual-performance Subscale at 5y, Group differences** Q1 (Ref) vs Q2: B: 0.83, 95% CI: -1.11, 2.77, P>0.05 **Q1 (Ref) vs Q3: B: 2.21, 95% CI: 0.30, 4.12, P<0.05** **Q1 (Ref) vs Q4: B: 1.99, 95% CI: 0.02, 3.95, P<0.05** **P trend=0.04**
	Maternal <u>small fatty fish</u> consumption during 3rd trimester modeled continuously in 10 g/wk increments (N=1567)	**MSCA General Cognitive Scale at 5y** B: -0.03, 95% CI: -0.11, 0.06, P>0.05 **Perceptual-performance Subscale at 5y** B: 0.00, 95% CI: -0.09, 0.09, P>0.05

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study; INMA; Spain** **(Continued)**	Maternal small fatty fish consumption during 3rd trimester in quartiles: Q1 (Ref, None, N=678) vs Q2 (Median=41 g/wk, N=259) vs Q3 (Median=72 g/wk, N=338) vs Q4 (Median=142 g/wk, N=290)	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: -0.70, 95% CI: -2.67, 1.26, P>0.05 Q1 (Ref) vs Q3: B: -0.41, 95% CI: -2.18, 1.36, P>0.05 Q1 (Ref) vs Q4: B: 0.21, 95% CI: -1.63, 2.05, P>0.05 P trend=0.88 **Perceptual-performance Subscale at 5y, Group differences** Q1 (Ref) vs Q2: B: -1.20, 95% CI: -3.21, 0.80, P>0.05 Q1 (Ref) vs Q3: B: 0.18, 95% CI: -1.62, 1.99, P>0.05 Q1 (Ref) vs Q4: B: 0.67, 95% CI: -1.21, 2.54, P>0.05 P trend=0.43
	Maternal lean fish consumption during 3rd trimester modeled continuously in 10 g/wk increments (N=1567)	**MSCA General Cognitive Scale at 5y** B: 0.01, 95% CI: -0.03, 0.05, P>0.05 **Perceptual-performance Subscale at 5y** B: 0.02, 95% CI: -0.02, 0.06, P>0.05
	Maternal lean fish consumption during 3rd trimester in quartiles: Q1 (Ref, Median=97 g/wk, N=332) vs Q2 (Median=193 g/wk, N=319) vs Q3 (Median=267 g/wk, N=305) vs Q4 (Median=390 g/wk, N=313) vs Q5 (Median=561 g/wk, N=296)	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: -0.54, 95% CI: -2.61, 1.52, P>0.05 Q1 (Ref) vs Q3: B: 0.35, 95% CI: -1.76, 2.46, P>0.05 Q1 (Ref) vs Q4: B: 0.08, 95% CI: -2.04, 2.20, P>0.05 Q1 (Ref) vs Q5: B: 0.54, 95% CI: -1.64, 2.71, P>0.05 P trend=0.50 **Perceptual-performance Subscale at 5y, Group differences** Q1 (Ref) vs Q2: B: -1.03, 95% CI: -3.13, 1.08, P>0.05 Q1 (Ref) vs Q3: B: 0.54, 95% CI: -1.61, 2.69, P>0.05 Q1 (Ref) vs Q4: B: 0.80, 95% CI: -1.35, 2.95, P>0.05 Q1 (Ref) vs Q5: B: 0.72, 95% CI: -1.49, 2.94, P>0.05 P trend=0.22
	Maternal shellfish consumption during 3rd trimester modeled continuously in 10 g/wk increments (N=1567)	**MSCA General Cognitive Scale at 5y** B: -0.07, 95% CI: -0.19, 0.04, P>0.05 **Perceptual-performance Subscale at 5y** B: -0.07, 95% CI: -0.19, 0.04, P>0.05

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study;** **INMA; Spain** **(Continued)**	Maternal <u>shellfish</u> consumption during 3rd trimester in quartiles: Q1 (Ref, None, N=301) vs Q2 (Median=24 g/wk, N=308) vs Q3 (Median=46 g/wk, N=320) vs Q4 (Median=73 g/wk, N=320) vs Q5 (Median=133 g/wk, N=316)	**MSCA General Cognitive Scale at 5y, Group differences** Q1 (Ref) vs Q2: B: 0.23, 95% CI: -2.07, 2.53, P>0.05 Q1 (Ref) vs Q3: B: -1.33, 95% CI: -3.46, 0.81, P>0.05 Q1 (Ref) vs Q4: B: 0.00, 95% CI: -2.11, 2.12, P>0.05 Q1 (Ref) vs Q5: B: -1.53, 95% CI: -3.67, 0.60, P>0.05 P trend=0.17 **Perceptual-performance Subscale at 5y, Group differences** Q1 (Ref) vs Q2: B: -0.26, 95% CI: -2.60, 2.08, P>0.05 Q1 (Ref) vs Q3: B: -1.27, 95% CI: -3.44, 0.90, P>0.05 Q1 (Ref) vs Q4: B: 0.52, 95% CI: -1.63, 2.68, P>0.05 Q1 (Ref) vs Q5: B: -1.73, 95% CI: -3.91, 0.44, P>0.05 P trend=0.19
The New Bedford Cohort		
Sagiv, 2012[20] **Prospective Cohort Study;** **The New Bedford Cohort; U.S.** ***Summary:*** *Maternal fish consumption during pregnancy was not associated with performance on the Continuous Performance Test or the processing speed and freedom from distractibility subscales of the WISC-III.*	Maternal <u>total seafood</u> intake (svg/wk) during pregnancy: ≤2 svg/wk (Ref) (N=248) vs >2 svg/wk (N=267)	*Shorter reaction time, lower reaction time variability, and fewer errors of omission and commission on the Continuous Performance Test (CPT) indicate better child performance* **CPT Mean reaction time at 8y, Group differences** ≤2 (Ref) vs >2 svg/wk: B: 7.7 ms, 95% CI: -3.8, 19.3, P=NR ≤2 (Ref) vs >2 svg/wk: B: 10.1 ms, 95% CI: -3.9, 24.1, P=NR (adjusted for maternal hair Hg) **CPT Reaction time variability at 8y, Group differences** ≤2 (Ref) vs >2 svg/wk: B: 1.5 ms, 95% CI: -3.6, 6.7, P=NR ≤2 (Ref) vs >2 svg/wk: B: -0.5 ms, 95% CI: -6.3, 5.4, P=NR (adjusted for maternal hair Hg) **CPT Errors of omission at 8y, Rate ratio** ≤2 (Ref) vs >2 svg/wk: RR: 1.0, 95% CI: 0.8, 1.3, P=NR ≤2 (Ref) vs >2 svg/wk: RR: 0.9, 95% CI: 0.7, 1.2, P=NR (adjusted for maternal hair Hg) **CPT Errors of commission at 8y, Rate ratio** ≤2 (Ref) vs >2 svg/wk: RR: 1.1, 95% CI: 1.0, 1.3, P=NR ≤2 (Ref) vs >2 svg/wk: RR: 1.1, 95% CI: 0.9, 1.3, P=NR (adjusted for maternal hair Hg)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Sagiv, 2012 **Prospective Cohort Study;** **The New Bedford Cohort; U.S.** **(Continued)**		*Higher scores on the Wechsler Intelligence Scale for Children (WISC-III) subscales indicate better child performance* **WISC-III Processing speed at 8y, Group differences** ≤2 (Ref) vs >2 svg/day: B: 1.3, 95% CI: -1.2, 3.8, P=NR ≤2 (Ref) vs >2 svg/day: B: 2.0, 95% CI: -0.8, 4.8, P=NR (adjusted for maternal hair Hg) **WISC-III Freedom from distractibility at 8y, Group differences** ≤2 (Ref) vs >2 svg/day: B: 0.3, 95% CI: -1.9, 2.6, P=NR ≤2 (Ref) vs >2 svg/day: B: 1.5, 95% CI: -1.1, 4.0, P=NR (adjusted for maternal hair Hg)
Other Prospective Cohorts		
Deroma, 2013[3] **Prospective Cohort Study;** **Italy** ***Summary:*** *Fish intake during pregnancy was not associated with Full Scale IQ, verbal IQ or performance IQ at 7y.*	Maternal fresh seafood (including fish, crustaceans, mollusks, tuna, mackerel, and sardines in oil) intake (svg/wk) during pregnancy modeled continuously (N=154)	*Higher scores on the Wechsler Intelligence Scale for Children (WISC-III) indicate better child performance* **WISC III Full Scale IQ at 7y** B: 1.29, P=0.32 (adjusted for maternal hair total Hg at delivery) B: 1.16, P=0.43 (adjusted for maternal hair total Hg at delivery + child total hair Hg at follow-up) **WISC III Verbal IQ at 7y** B: 0.34, P=0.81 (adjusted for maternal hair total Hg at delivery) B: -0.07, P=0.96 (adjusted for maternal hair total Hg at delivery + child total hair Hg at follow-up) **WISC III Performance IQ at 7y** B: 1.89, P=0.15 (adjusted for maternal hair total Hg at delivery) B: 2.12, P=0.15 (adjusted for maternal hair total Hg at delivery + child total hair Hg at follow-up)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Deroma, 2013 **Prospective Cohort Study;** **Italy** **(Continued)**	Maternal canned seafood (including fish, crustaceans, mollusks, tuna, mackerel, and sardines in oil) intake (svg/wk) during pregnancy modeled continuously (N=154)	**WISC III Full Scale IQ at 7y** B: -2.50, P=0.19 (adjusted for maternal hair total Hg at delivery) B: -2.42, P=0.22 (adjusted for maternal hair total Hg at delivery + child total hair Hg at follow-up) **WISC III Verbal IQ at 7y** B: -0.86, P=0.67 (adjusted for maternal hair total Hg at delivery) B: -0.82, P=0.70 (adjusted for maternal hair total Hg at delivery + child total hair Hg at follow-up) **WISC III Performance IQ at 7y** B: -3.67, P=0.05 (adjusted for maternal hair total Hg at delivery) B: -3.61, P=0.07 (adjusted for maternal hair total Hg at delivery + child total hair Hg at follow-up)
Gale, 2008[5] **Prospective Cohort Study** **U.K.** ***Summary:*** *Maternal fish intake during pregnancy not associated with child cognitive outcomes at 9y except for maternal oily fish intake in early pregnancy, which was associated with reduced risk of hyperactivity symptoms, and maternal total fish intake in late pregnancy, which was associated with higher verbal IQ scores.*	Maternal total seafood intake in early pregnancy: Never (Ref, N=19) vs <1x/wk (N=55) vs 1-2x/wk (N=102) vs ≥3x/wk (N=41)	*Higher scores on the Strengths and Difficulties Questionnaire (SDQ) total difficulties score and its subscales indicate worse behavioral outcomes. Data dichotomized as 10-20% with worst behavioral symptoms/highest scores and all others (reference)* **SDQ Total Difficulties Score at 9y** Never (Ref) vs <1x/wk: Data NR Never (Ref) vs 1-2x/wk: OR: 0.32, 95% CI: 0.08, 1.26, P=NR Never (Ref) vs ≥3x/wk: OR: 0.23, 95% CI: 0.04, 1.24, P=NR No association between frequency of seafood intake in early pregnancy and risk of high scores on the Hyperactivity, Conduct Problems, Peer Problems, or Emotional Symptoms Subscales (Data NR; Only unadjusted analyses reported)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Gale, 2008 **Prospective Cohort Study** **U.K.** **(Continued)**	Maternal <u>total seafood</u> intake in early pregnancy: Never (Ref, N=19) vs <1x/wk (N=55) vs 1-2x/wk (N=102) vs ≥3x/wk (N=41)	*Higher scores on the Wechsler Abbreviated Scale of Intelligence (WASI) Full Scale IQ and Performance and Verbal IQ indicate better child cognitive development* **WASI Full Scale IQ at 9y, Group Differences** Never (Ref) vs <1x/wk: B: 5.12, 95% CI: -1.95, 12.2, P=NR Never (Ref) vs 1-2x/wk: B: 3.07, 95% CI: -3.74, 9.88, P=NR Never (Ref) vs ≥3x/wk: B: 1.19, 95% CI: -6.24, 8.61, P=NR **Performance IQ at 9y** <u>No association</u> between frequency of seafood intake in early pregnancy and performance IQ (Data NR) **Verbal IQ at 9y** <u>No association</u> between frequency of seafood intake in early pregnancy and verbal IQ (Data NR)
	Maternal <u>total seafood</u> intake in late pregnancy: Never (Ref, N=19) vs <1x/wk (N=42) vs 1-2x/wk (N=108) vs ≥3x/wk (N=48)	**SDQ Total Difficulties Score at 9y** Never (Ref) vs <1x/wk: P=NS (Data NR) Never (Ref) vs 1-2x/wk: P=NS (Data NR) Never (Ref) vs ≥3x/wk: P=NS (Data NR) <u>No association</u> between frequency of seafood intake in late pregnancy and risk of high scores on the Hyperactivity, Conduct Problems, Peer Problems, or Emotional Symptoms Subscales (Data NR; Only unadjusted analyses reported)
		WASI Full Scale IQ at 9y, Group Differences **Never (Ref) vs <1x/wk: B: 7.76, 95% CI: 0.38, 15.1, P=NR** **Never (Ref) vs 1-2x/wk: B: 6.91, 95% CI: 0.19, 13.6, P=NR** Never (Ref) vs ≥3x/wk: B: 5.86, 95% CI: -1.55, 13.3, P=NR **Performance IQ at 9y, Group Differences** <u>No association</u> between frequency of seafood intake in late pregnancy and performance IQ (Data NR) **Verbal IQ at 9y, Group Differences** Never (Ref) vs <1x/wk: B: 7.66, 95% CI: -0.1, 15.4, P=NR **Never (Ref) vs 1-2x/wk: B: 7.32, 95% CI: 0.26, 14.4, P=NR** **Never (Ref) vs ≥3x/wk: B: 8.07, 95% CI: 0.28, 15.9, P=NR**

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Gale, 2008 **Prospective Cohort Study** **U.K.** **(Continued)**	Maternal <u>seafood</u> intake in late pregnancy: Never (Ref, N=19) vs Any (N=198)	**WASI Verbal IQ at 9y, Group Differences** **Never (Ref) vs Any: B: 7.55, 95% CI: 0.75, 14.4, P=NR**
	Maternal <u>oily fish</u> intake in early pregnancy: Never (Ref, N=62) vs <1x/wk (N=100) vs ≥1x/wk (N=55)	**SDQ Total Difficulties Score at 9y** Never (Ref) vs <1x/wk: OR: 1.23, 95% CI: 0.41, 3.66, P=NR Never (Ref) vs ≥1x/wk: OR: 0.83, 95% CI: 0.22, 3.04, P=NR **Hyperactivity Subscale at 9y** **Never (Ref) vs <1x/wk: OR: 0.30, 95% CI: 0.12, 0.76, P=NR** Never (Ref) vs ≥1x/wk: OR: 0.41, 95% CI: 0.15, 1.12, P=NR **Conduct Problems Subscale at 9y** Never (Ref) vs <1x/wk: OR: 0.58, 95% CI: 0.22, 1.53, P=NR Never (Ref) vs ≥1x/wk: OR: 0.36, 95% CI: 0.11, 1.21, P=NR **Peer Problems Subscale at 9y** Never (Ref) vs <1x/wk: OR: 0.79, 95% CI: 0.27, 2.32, P=NR Never (Ref) vs ≥1x/wk: OR: 1.44, 95% CI: 0.47, 4.80, P=NR **Emotional Symptoms Subscale at 9y** Never (Ref) vs <1x/wk: OR: 0.63, 95% CI: 0.19, 2.06, P=NR Never (Ref) vs ≥1x/wk: OR: 0.79, 95% CI: 0.20, 3.08, P=NR
		WASI Full Scale IQ at 9y, Group Differences Never (Ref) vs <1x/wk: B: 2.52, 95% CI: -1.89, 6.94, P=NR Never (Ref) vs ≥1x/wk: B: -0.99, 95% CI: -6.01, 4.02, P=NR **Performance IQ** <u>No association</u> between frequency of oily fish intake in early pregnancy and performance IQ (Data NR) **Verbal IQ** <u>No association</u> between frequency of oily fish intake in early pregnancy and verbal IQ (Data NR)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Gale, 2008 **Prospective Cohort Study** **U.K.** **(Continued)**	Maternal <u>oily</u> fish intake in early pregnancy: Never (Ref, N=62) vs Any (N=155)	**SDQ Hyperactivity Subscale at 9y** **Never (Ref) vs Any: OR: 0.34, 95% CI: 0.15, 0.78, P=NR**
	Maternal <u>oily fish</u> intake in late pregnancy: Never (Ref, N=70) vs <1x/wk (N=97) vs ≥1x/wk (N=50)	**SDQ Total Difficulties Scale at 9y** Never (Ref) vs <1x/wk: OR: 1.25, 95% CI: 0.43, 3.60, P=NR Never (Ref) vs ≥1x/wk: OR: 1.20, 95% CI: 0.32, 4.49, P=NR **Hyperactivity Subscale at 9y** **Never (Ref) vs <1x/wk: OR: 0.40, 95% CI: 0.16, 0.98, P=NR** Never (Ref) vs ≥1x/wk: OR: 0.72, 95% CI: 0.26, 1.98, P=NR **Conduct Problems Subscale at 9y** Never (Ref) vs <1x/wk: OR: 0.46, 95% CI: 0.18, 1.17, P=NR Never (Ref) vs ≥1x/wk: OR: 0.31, 95% CI: 0.08, 1.10, P=NR **Peer Problems Subscale at 9y** Never (Ref) vs <1x/wk: OR: 0.68, 95% CI: 0.25, 1.82, P=NR Never (Ref) vs ≥1x/wk: OR: 0.82, 95% CI: 0.27, 2.57, P=NR **Emotional Symptoms Subscale at 9y** Never (Ref) vs <1x/wk: OR: 2.32, 95% CI: 0.73, 7.43, P=NR Never (Ref) vs ≥1x/wk: OR: 1.04, 95% CI: 0.23, 4.66, P=NR
		WASI Full Scale IQ at 9y, Group Differences Never (Ref) vs <1x/wk: B: 3.43, 95% CI: -0.80, 7.65, P=NR Never (Ref) vs ≥1x/wk: B: -0.29, 95% CI: -5.34, 4.76, P=NR **Performance IQ** <u>No association</u> between frequency of oily fish intake in late pregnancy and performance IQ (Data NR) **Verbal IQ** <u>No association</u> between frequency of oily fish intake in late pregnancy and verbal IQ (Data NR)
	Maternal <u>oily fish</u> intake in late pregnancy: Never (Ref, N=70) vs Any (N=147)	**Hyperactivity Subscale at 9y** Never (Ref) vs Any: OR: 0.49, 95% CI: 0.22, 1.10, P=NR

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Hisada, 2017[8] **Prospective Cohort Study** **Japan** ***Summary:*** *Higher frequency of fish consumption during pregnancy was associated with better child development and behavior.*	Maternal seafood intake during pregnancy: Less frequent eater (Ref) vs frequent eater (N=88)	*Higher scores on the Kinder Infant Development Scale (KIDS) and its subscales indicate better child development and behavior* **Developmental Quotient at 18mo, Group Difference** **Less frequent eater (Ref) vs Frequent eater: B: 7.77, 95% CI: 1.65, 13.90, Standardized B: 0.263, P=0.013** **Physical motor Subscale at 18mo** **Less frequent eater (Ref) vs Frequent eater: Positive association, P<0.05, Data NR** **Manipulation Subscale at 18mo** **Less frequent eater (Ref) vs Frequent eater: Positive association, P<0.05, Data NR** **Receptive language Subscale at 18mo** Less frequent eater (Ref) vs Frequent eater: P>0.05, Data NR **Expressive language Subscale at 18mo** Less frequent eater (Ref) vs Frequent eater: P>0.05, Data NR **Language concepts Subscale at 18mo** Less frequent eater (Ref) vs Frequent eater: P>0.05, Data NR **Social relationships with children Subscale at 18mo** Less frequent eater (Ref) vs Frequent eater: P>0.05, Data NR **Social relationships with adults Subscale at 18mo** Less frequent eater (Ref) vs Frequent eater: P>0.05, Data NR **Discipline Subscale at 18mo** Less frequent eater (Ref) vs Frequent eater: P>0.05, Data NR **Feeding Subscale at 18mo** Less frequent eater (Ref) vs Frequent eater: P>0.05, Data NR

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Hu, 2016[9] **Prospective Cohort Study** **China** ***Summary:*** *Maternal fish consumption during pregnancy was positively associated with the adaptive domain of the GDS at 1y. No associations between the 4 other domains of the GDS and maternal fish consumption during pregnancy were detected.*	Maternal frequency of total fish intake during pregnancy: Never or monthly (N=114) vs at least twice a month (N=162) vs at least once a wk (N=134)	*Higher development quotient (DQ) scores on the Gesell developmental schedules (GDS) domains at 1y indicate greater neurodevelopment* **Gross motor domain at 1y, Mean raw scores** Never or monthly: 103.67, SD=8.24 At least 2 x/mo: 102.95, SD=8.17 At least 1 x/wk: 103.91, SD=9.15, Group differences, P=0.69 **Fine motor domain 1y, Mean raw scores** Never or monthly: 114.48, SD=9.30 At least 2 x/mo: 111.92, SD=9.57 At least 1 x/wk: 112.77, SD=8.94 Group differences, P=0.48 **Adaptive domain 1y, Mean raw scores** **Never or monthly: 101.19, SD=4.60** **At least 2 x/mo: 102.58, SD=6.42** **At least 1 x/wk: 109.77, SD=8.94** **Group differences, P= 0.02** **Language domain 1y, Mean raw scores** Never or monthly: 97.34, SD=6.12 At least 2 x/mo: 96.81, SD=5.55 At least 1 x/wk: 97.60, SD=7.88 Group differences, P=0.57 **Social domain 1y, Mean raw scores** Never or monthly: 101.27, SD=6.20 At least 2 x/mo: 100.93, SD=5.27 At least 1 x/wk: 102.35, SD=6.78 Group differences, P=0.17

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Lederman, 2008[11] **Prospective Cohort Study** **U.S.** ***Summary:*** *Prenatal fish/seafood intake associated with higher Full Scale IQ and Verbal IQ at 48 mo, and psychomotor development at 36mo. No associations between prenatal fish/seafood intake and child developmental outcomes at 12mo and 24mo detected.*	Maternal consumption of fish/seafood during pregnancy: None (Ref) vs Any (12mo, N=132; 24mo, N=131; 36mo, N=114; 48mo, N=107)	*Higher scores on the Mental Development Index (MDI) and Psychomotor Development Index (PDI) for the Bayley Scales of Infant Development (BSID-II) indicate better child development* **BSID-II MDI at 12mo, Group differences** None (Ref) vs Any: B: 2.49, P=0.192 (adjusted for natural log cord mercury) **BSID-II PDI at 12mo, Group differences** None (Ref) vs Any: B: 2.36, P=0.408 (adjusted for natural log cord mercury)
	Maternal consumption of fish/seafood during pregnancy: None (Ref) vs Any (12mo, N=132; 24mo, N=131; 36mo, N=114; 48mo, N=107)	**BSID-II MDI at 24mo, Group differences** None (Ref) vs Any: B: 2.99, P=0.231 (adjusted for natural log cord mercury) **BSID-II PDI at 24mo, Group differences** None (Ref) vs Any: B: 4.58 P=0.070 (adjusted for natural log cord mercury)
		BSID-II MDI at 36mo, Group differences None (Ref) vs Any: B: 4.13, P=0.092 (adjusted for natural log cord mercury) **BSID-II PDI at 36mo, Group differences** **None (Ref) vs Any: B: 9.22, P=0.005** (adjusted for natural log cord mercury)
		Higher scores on the Wechsler Preschool & Primary Scales of Intelligence (WPPSI-R) Full Scale IQ and Performance and Verbal IQ indicate better child cognitive development **WPPSI-R Full Scale IQ at 48mo, Group differences** **None (Ref) vs Any: B: 5.54, P=0.019** (adjusted for natural log cord mercury) **Performance IQ at 48mo, Group differences** None (Ref) vs Any: B: 4.07, P=0.161 (adjusted for natural log cord mercury) **Verbal IQ at 48mo, Group differences** **None (Ref) vs Any: B: 5.60, P=0.025** (adjusted for natural log cord mercury)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Mendez, 2009[13] **Prospective Cohort Study** **Spain** ***Summary:*** *Prenatal fish intake >2-3 x/wk, but not >3x/wk, was associated with better performance on a variety of cognitive domains at 4y in children breastfed <6mo. No association was found between prenatal fish intake and cognition in children breastfed >=6mo. Prenatal intake of other seafood (including shellfish and squid) >1x/wk was associated with worse performance on a variety of cognitive domains at 4y.*	Maternal fish and other seafood intake during pregnancy (N=392): <1.5 x/wk (Ref, N=NR) vs ≥1.5-2 x/wk (N=NR) vs >2-3 x/wk (N=NR) vs >3 x/wk (N=NR)	*Higher scores on the McCarthy Scales of Children's Abilities (MSCA) general cognitive scale and its subscales indicate better cognitive development* **MSCA General Cognitive Scale at 4y, Group differences** ≤1.5 (Ref) vs ≥1.5-2 x/wk: B: 0.11, P>0.05 ≤1.5 (Ref) vs >2-3 x/wk: B: -0.47, P>0.05 ≤1.5 (Ref) vs >3 x/wk: B: -3.12, P>0.05
	Maternal fish intake during pregnancy (N=392): <1.5 x/wk (Ref, N=NR) vs ≥ 1.5-2 x/wk (N=NR) vs >2-3 x/wk (N=NR) vs >3 x/wk (N=NR)	**MSCA General Cognitive Scale at 4y, Group differences** ≤1.5 (Ref) vs ≥1.5-2 x/wk: B: -0.33, P>0.05 **≤1.5 (Ref) vs >2-3 x/wk: B: 4.68, P<0.05** ≤1.5 (Ref) vs 3 x/wk: B: -4.09, P>0.05

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Mendez, 2009 **Prospective Cohort Study** **Spain** **(Continued)**	Maternal fish intake during pregnancy: ≤ 1 x/wk (Ref, N=NR) vs >1-2 x/wk (N=NR) vs >2-3 x/wk (N=NR) vs >3x/wk (N=NR) Subsample BF <6mo: N=234	**MSCA General Cognitive Scale at 4y, Group differences** <1 (Ref) vs >1-2 x/wk: B: 2.7, 95% CI: -1.2, 6.5, P>0.05 **<1 (Ref) vs >2-3 x/wk: B: 11.0, 95% CI: 5.0, 17.1, P<0.05** <1 (Ref) vs >3 x/wk: B: -1.2, 95% CI: -9.8, 7.3, P>0.05 **Perceptual Performance Subscale at 4y, Group differences** <1 (Ref) vs >1-2 x/wk: B: 2.3, 95% CI: -1.5, 6.1, P>0.05 **<1 (Ref) vs >2-3 x/wk: B: 10.0, 95% CI: 4.1, 16.0, P<0.05** <1 (Ref) vs >3 x/wk: B: 1.5, 95% CI: -7.0, 9.9, P>0.05 **Memory Subscale at 4y, Group differences** <1 (Ref) vs >1-2 x/wk: B: 2.0, 95% CI: -2.1, 6.1, P>0.05 **<1 (Ref) vs >2-3 x/wk: B: 10.5, 95% CI: 4.1, 16.9, P<0.05** <1 (Ref) vs >3 x/wk: B: -3.3, 95% CI: -12.4, 5.8, P>0.05 **Verbal Subscale at 4y, Group differences** <1 (Ref) vs >1-2 x/wk: B: 2.2, 95% CI: -1.8, 6.3, P>0.05 **<1 (Ref) vs >2-3 x/wk: B: 9.9, 95% CI: 3.5, 16.2, P<0.05** <1 (Ref) vs >3 x/wk: B: -1.8, 95% CI: -10.8, 7.2, P>0.05 **Numeric Subscale a 4y, Group differences** <1 (Ref) vs >1-2 x/wk: B: 2.1, 95% CI: -1.8, 6.0, P>0.05 **<1 (Ref) vs >2-3 x/wk: B: 6.8, 95% CI: 0.7, 12.9, P<0.05** <1 (Ref) vs >3 x/wk: B: -3.3, 95% CI: -11.9, 5.4, P>0.05 **Motor Skills Subscale at 4y, Group differences** <1 (Ref) vs >1-2 x/wk: B: 2.1, 95% CI: -1.8, 6.0, P>0.05 **<1 (Ref) vs >2-3 x/wk: B: 6.7, 95% CI: 0.7, 12.8, P<0.05** <1 (Ref) vs >3 x/wk: B: -2.3, 95% CI: -10.9, 6.3, P>0.05

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Mendez, 2009 **Prospective Cohort Study** **Spain** **(Continued)**	Maternal fish intake during pregnancy: ≤ 1 x/wk (Ref, N=NR) vs >1-2 x/wk (N=NR) vs >2-3 x/wk (N=NR) vs >3x/wk (N=NR) Subsample BF ≥6mo: N=143	**MSCA General Cognitive Scale at 4y, Group differences** <1 (Ref) vs >1-2 x/wk: B: -0.7, 95% CI: -7.0, 5.7, P>0.05 <1 (Ref) vs >2-3 x/wk: B: -0.7, 95% CI: -8.3, 6.9, P>0.05 <1 (Ref) vs >3 x/wk: B: -5.3, 95% CI: -17.9, 7.3, P>0.05 **Perceptual Performance Subscale at 4y, Group differences** <1 (Ref) vs >1-2 x/wk: B: -0.2, 95% CI: -6.1, 6.6, P>0.05 <1 (Ref) vs >2-3 x/wk: B: 0.8, 95% CI: -6.8, 8.5, P>0.05 <1 (Ref) vs >3 x/wk: B: -0.2, 95% CI: -12.4, 12.9, P>0.05 **Memory Subscale at 4y, Group differences** <1 (Ref) vs >1-2 x/wk: B: -1.8, 95% CI: -8.2, 4.5, P>0.05 <1 (Ref) vs >2-3 x/wk: B: -4.6, 95% CI: -12.3, 3.3, P>0.05 **<1 (Ref) vs >3 x/wk: B: -12.7, 95% CI: -25.5, 0.0, P<0.05** **Verbal Subscale at 4y, Group differences** <1 (Ref) vs >1-2 x/wk: B: -1.1, 95% CI: -7.7, 5.4, P>0.05 <1 (Ref) vs >2-3 x/wk: B: -0.5, 95% CI: -8.3, 7.4, P>0.05 <1 (Ref) vs >3 x/wk: B: -8.2, 95% CI: -21.3, 4.9, P>0.05 **Numeric Subscale at 4y, Group differences** <1 (Ref) vs >1-2 x/wk: B: -0.5, 95% CI: -6.8, 5.9, P>0.05 <1 (Ref) vs >2-3 x/wk: B: -3.1, 95% CI: -10.7, 4.6, P>0.05 <1 (Ref) vs >3 x/wk: B: -2.8, 95% CI: -15.5, 9.9, P>0.05 **Motor Skills Subscale at 4y, Group differences** <1 (Ref) vs >1-2 x/wk: B: -2.1, 95% CI: -8.5, 4.3, P>0.05 <1 (Ref) vs >2-3 x/wk: B: -0.8, 95% CI: -8.5, 7.0, P>0.05 <1 (Ref) vs >3 x/wk: B: -2.1, 95% CI: -14.8, 10.7, P>0.05
	Maternal shellfish and squid intake during pregnancy (N=392): <0.5 x/wk (Ref, N=NR) vs ≥0.5-1 x/wk (N=NR) vs >1-2 x/wk (N=NR) vs >2 x/wk (N=NR)	**MSCA General Cognitive Scale at 4y, Group differences** ≤0.5 (Ref) vs ≥0.5-1 x/wk: B: -1.29 P>0.05 **≤0.5 (Ref) vs >1-2 x/wk: B: -5.39 P<0.05** ≤0.5 (Ref) vs >2 x/wk: B: -3.02 P>0.05

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Mendez, 2009 **Prospective Cohort Study** **Spain** **(Continued)**	Maternal shellfish and squid intake during pregnancy: ≤0.5 x/wk (Ref, N=115) vs >0.5-1 x/wk (N=107) vs >1 x/wk (N=155)	**MSCA General Cognitive Scale at 4y, Group differences** ≤0.5 (Ref) vs >0.5-1 x/wk: B: -1.0, 95% CI: -4.7, 2.6, P>0.05 **≤0.5 (Ref) vs >1 x/wk: B: -5.2, 95% CI: -8.8, -1.7, P<0.05** **Perceptual Performance Subscale at 4y, Group differences** ≤0.5 (Ref) vs >0.5-1 x/wk: B: -2.4, 95% CI: -6.0, 1.3, P>0.05 **≤0.5 (Ref) vs >1 x/wk: B: -5.0, 95% CI: -8.5, -1.5, P<0.05** **Memory Subscale at 4y, Group differences** ≤0.5 (Ref) vs >0.5-1 x/wk: B: 0.9, 95% CI: -3.0, 4.7, P>0.05 ≤0.5 (Ref) vs >1 x/wk: B: -3.5, 95% CI: -7.2, 0.2, P>0.05 **Verbal Subscale at 4y, Group differences** ≤0.5 (Ref) vs >0.5-1 x/wk: B: 0.3, 95% CI: -3.6, 4.1, P>0.05 **≤0.5 (Ref) vs >1 x/wk: B: -3.7, 95% CI: -7.4, -0.0, P<0.05** **Numeric Subscale at 4y, Group differences** ≤0.5 (Ref) vs >0.5-1 x/wk: B: -1.3, 95% CI: -5.0, 2.4, P>0.05 **≤0.5 (Ref) vs >1 x/wk: B: -5.2, 95% CI: -8.8, -1.6, P<0.05** **Motor Skills Subscale at 4y, Group differences** ≤0.5 (Ref) vs >0.5-1 x/wk: B: -1.1, 95% CI: -4.7, 2.6, P>0.05 ≤0.5 (Ref) vs >1 x/wk: B: -2.2, 95% CI: -5.7, 1.4, P>0.05

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Normia, 2019[15] **Prospective Cohort Study** **Finland** ***Summary:*** *Maternal fish intake during the 3rd trimester was not significantly associated with pVEP amplitude or latency.*	Maternal frequency of fish consumption 2wk prior to the 3rd trimester of pregnancy: 0-2 x/wk vs ≥3 x/wk; N=19 (N by intake group NR)	*Higher amplitudes and shorter latencies of pattern-reversal visual evoked potentials (pVEP) indicate greater neurodevelopment within the visual system* **pVEP 60′ amplitude at 2y, Group differences** 0-2 x/wk: Mean: 15.0 µV, SD=4.8 ≥3 x/wk: Mean: 23.4 µV, SD=8.1 P=0.058 **pVEP 30′ amplitude at 2y, Group differences** 0-2 x/wk: Mean: 13.4 µV, SD=2.0 ≥3 x/wk: Mean: 20.4 µV, SD=6.7 P=0.07 **pVEP 60′ and 30' latencies at 2y, Group differences** No association between maternal fish intake (0-2 vs ≥3 x/wk) and pVEP 60' or 30' latencies (data NR)

[vi] 1 oz = 28.3 grams
[vii] Abbreviations: B – beta, BF – breastfeeding, CI – confidence interval, g – gram(s), Hg – mercury, MeHg – methyl mercury, mo – month(s), NR – not reported, OR – odds ratio, oz – ounce(s), Ref – reference group, SD – standard deviation, SE – standard error, svg – serving(s), vs – versus, wk – week(s), x – time(s), y – year(s)

Table 3. Results from studies that examined the relationship between seafood consumption during pregnancy and neurocognitive development in the child (Attention-Deficit/Hyperactivity Disorder [ADHD]- and Autism Spectrum Disorder [ASD]-like traits or behaviors, and ASD diagnosis)[viii,ix]

Article	Exposure	Outcome and Results (statistically significant results are bolded)
ADHD-Like Behaviors or Traits		
Hibbeln, 2007[7] **Prospective Cohort Study** **ALSPAC; U.K.** **Note: Full SDQ results presented in Table 1** ***Summary:*** *No statistically significant association between maternal fish intake and child hyperactivity was detected.*	Maternal seafood intake at 32wk gestation: >340 g/wk (Ref) vs None vs 1-340 g/wk N~6580 at 7y	*Lower scores on the Strengths and Difficulties Questionnaire (SDQ) hyperactivity subscale indicate better child behavior* **Note: Full SDQ results presented in Table 1** **SDQ Hyperactivity at 7y, OR for sub-optimum behavioral outcomes (highest ~10%)** >340 (Ref) vs 0 g/wk: OR: 1.13, 95% CI: 0.84, 1.53 >340 (Ref) vs 1-340 g/wk: OR: 0.91, 95% CI: 0.73, 1.12 P trend: 0.63
Mesirow, 2017[14] **Prospective Cohort Study** **ALSPAC; U.K.** **Note: Full SDQ results presented in Table 1** ***Summary:*** *No association between maternal fish intake and child hyperactivity at 4-10y or 12-13y was detected for either children with early-onset conduct problems (EOP) or children with low conduct problems.*	Maternal seafood intake during pregnancy by conduct problem trajectory (Early-onset persistent conduct problems, EOP; Low conduct problems, Low CP) at 32wk gestation: <2 svg/wk vs ≥2 svg/wk N=5493 (N by intake group NR)	*Lower scores on the Strengths and Difficulties Questionnaire (SDQ) hyperactivity subscale indicate less impairment* **Note: Full SDQ results presented in Table 1** **SDQ Hyperactivity Subscale at 4-10y, Group differences** <2 vs ≥2 svg/wk: F: 1.01, Effect size: 0.06, P>0.05 Interaction of fish intake by conduct problem trajectory: F: 0.82, P>0.05 EOP, <2 vs ≥2 svg/wk: Mean: 0.87, SE=0.04 vs Mean: 0.80, SE=0.06, Effect size: 0.10 Low CP, <2 vs ≥2 svg/wk: Mean: -0.29, SE=0.02 vs Mean: -0.29, SE=0.02, Effect size: 0.01 **SDQ Hyperactivity Subscale at 12-13y, Group differences** <2 vs ≥2 svg/wk: F: 0.14, Effect size: 0.06 P>0.05 Interaction of fish intake by conduct problem trajectory: F: 0.00, P>0.05 EOP, <2 vs ≥2 svg/wk: Mean: 0.90, SE=0.04 vs Mean: 0.88, SE=0.06, Effect size: 0.03 Low CP, <2 vs ≥2 svg/wk: Mean: -0.24, SE=0.02 vs Mean: -0.26, SE=0.02, Effect size: 0.03

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Sagiv, 2012[20] **Prospective Cohort Study** **The New Bedford Cohort; U.S.** ***Summary:*** *Maternal fish consumption >2 svg/wk during pregnancy was associated with lower risk of ADHD-like behaviors at 8y compared to ≤2 svg/wk.*	Maternal total seafood intake during pregnancy: ≤2 svg/wk (Ref) (N=245) vs >2 svg/wk N=260 for Inattentive and total subtype N=266 for Impulsive/Hyperactive	*Higher scores on the Conners' Rating Scale-Teachers (CRS-T) subscales indicate more adverse behavior* **CRS-T Inattentive subscale mild/markedly atypical scores (>86th %ile) at 8y** **≤2 (Ref) vs >2 svg/wk: RR: 0.6, 95% CI: 0.4, 0.8, P=NR** **≤2 (Ref) vs >2 svg/wk: RR: 0.6, 95% CI: 0.4, 0.9, P=NR** (adjusted for maternal hair THg) **CRS-T Impulsive/Hyperactive subscale mild/markedly atypical scores (>86th %ile) at 8y** **≤2 (Ref) vs >2 svg/wk: RR: 0.4, 95% CI: 0.2, 0.6, P=NR** **≤2 (Ref) vs >2 svg/wk: RR: 0.4, 95% CI: 0.2, 0.6, P=NR** (adjusted for maternal hair THg) **CRS-T Total (subtypes combined) subscale mild/markedly atypical scores (>86th %ile) at 8y** **≤2 (Ref) vs >2 svg/wk: RR: 0.5, 95% CI: 0.4, 0.7, P=NR** **≤2 (Ref) vs >2 svg/wk: RR: 0.6, 95% CI: 0.4, 0.9, P=NR** (adjusted for maternal hair THg)
Gale, 2008[5] **Prospective Cohort Study** **U.K.** **Note: Full SDQ results presented in Table 1** ***Summary:*** *Maternal oily fish intake during early pregnancy was associated with reduced risk of hyperactivity symptoms at 9y. No additional associations between maternal oily fish intake or total fish intake and hyperactivity symptoms detected.*	Maternal total seafood intake in early pregnancy: Never (Ref, N=19) vs <1x/wk (N=55) vs 1-2x/wk (N=102) vs ≥3x/wk (N=41)	*Higher scores on the Strengths and Difficulties Questionnaire (SDQ) hyperactivity subscale indicate worse behavioral outcomes. Data dichotomized as 10-20% with worst behavioral symptoms/highest scores and all others (reference)* **Note: Full SDQ results presented in Table 1** No association between frequency of seafood intake in early pregnancy and risk of high scores on the Hyperactivity subscale at 9y (Data NR; Only unadjusted analyses reported)

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Gale, 2008 **Prospective Cohort Study** **U.K.** **(Continued)**	Maternal <u>total seafood</u> intake in late pregnancy: Never (Ref, N=19) vs <1x/wk (N=42) vs 1-2x/wk (N=108) vs ≥3x/wk (N=48)	<u>**Note: Full SDQ results presented in Table 1**</u> <u>No association</u> between frequency of seafood intake in late pregnancy and risk of high scores on the Hyperactivity subscale at 9y (Data NR; Only unadjusted analyses reported)
	Maternal <u>oily fish</u> intake in early pregnancy: Never (Ref, N=62) vs <1x/wk (N=100) vs ≥1x/wk (N=55)	<u>**Note: Full SDQ results presented in Table 1**</u> **SDQ Hyperactivity Subscale at 9y** **Never (Ref) vs <1x/wk: OR: 0.30, 95% CI: 0.12, 0.76, P=NR** Never (Ref) vs ≥1x/wk: OR: 0.41, 95% CI: 0.15, 1.12, P=NR
	Maternal <u>oily</u> fish intake in early pregnancy: Never (Ref, N=62) vs Any (N=155)	<u>**Note: Full SDQ results presented in Table 1**</u> **SDQ Hyperactivity Subscale at 9y** **Never (Ref) vs Any: OR: 0.34, 95% CI: 0.15, 0.78, P=NR**
	Maternal <u>oily fish</u> intake in late pregnancy: Never (Ref, N=70) vs <1x/wk (N=97) vs ≥1x/wk (N=50)	<u>**Note: Full SDQ results presented in Table 1**</u> **SDQ Hyperactivity Subscale at 9y** **Never (Ref) vs <1x/wk: OR: 0.40, 95% CI: 0.16, 0.98, P=NR** Never (Ref) vs ≥1x/wk: OR: 0.72, 95% CI: 0.26, 1.98, P=NR
	Maternal <u>oily fish</u> intake in late pregnancy: Never (Ref, N=70) vs Any (N=147)	<u>**Note: Full SDQ results presented in Table 1**</u> **SDQ Hyperactivity Subscale at 9y** Never (Ref) vs Any: OR: 0.49, 95% CI: 0.22, 1.10, P=NR

Article	Exposure	Outcome and Results (statistically significant results are bolded)
ASD-like Behaviors and Traits, or ASD Diagnoses		
Julvez, 2016[10] **Prospective Cohort Study** **INMA; Spain** ***Summary:*** *Seafood consumption during the 1st trimester had a beneficial association with child autism traits at 5y. Benefits were predominantly seen with small fatty fish, large fatty fish, and lean fish at moderate intake levels. No adverse associations were seen at the highest intake levels.*	Maternal total seafood consumption during 1st trimester in quintiles: Q1 (Ref, Median=195 g/wk, N=289) vs Q2 (Median=338 g/wk, N=294) vs Q3 (Median=461 g/wk, N=271) vs Q4 (Median=600 g/wk, N=280) vs Q5 (Median=854 g/wk N=260)	*Lower scores on the Childhood Asperger Syndrome Test (CAST) indicate lower amounts of Autistic traits* **CAST Score at 5y, Group differences** Q1 (Ref) vs Q2: B: -0.42, 95% CI: -0.90, 0.07, P>0.05 Q1 (Ref) vs Q3: B: -0.45, 95% CI: -0.95, 0.05, P>0.05 **Q1 (Ref) vs Q4: B: -0.61, 95% CI: -1.12, -0.11, P<0.05** **Q1 (Ref) vs Q5: B: -0.55, 95% CI: -1.06, -0.04, P<0.05** **P trend=0.04**
	Maternal total seafood consumption during 1st trimester in quintiles: Q1 (Ref ≤340 g/wk, Median=243 g/wk, N=446) vs Q2 (Median=370 g/wk, N=140) vs Q3 (Median=461 g/wk, N=280) vs Q4 (Median=600 g/wk, N=284) vs Q5 (Median=854 g/wk, N=262)	**CAST Score at 5y, ref group ≤340 g/wk, Group differences** Q1 (Ref) vs Q2: B: -0.03, 95% CI: -0.60, 0.54, P>0.05 Q1 (Ref) vs Q3: B: -0.25, 95% CI: -0.70, 0.21, P>0.05 Q1 (Ref) vs Q4: B: -0.41, 95% CI: -0.86, 0.05, P>0.05 Q1 (Ref) vs Q5: B: -0.34, 95% CI: -0.81, 0.12, P>0.05 P trend=0.08
	Maternal total seafood consumption during 1st trimester modeled continuously in 10 g/wk increments (N=1393)	**CAST Score at 5y** **B:-0.01, 95% CI: -0.01, -0.00, P<0.05**
	Maternal large fatty fish consumption during 1st trimester in quartiles: Q1 (Ref, Median=0 g/wk, N=613) vs Q2 (Median=48 g/wk, N=237) vs Q3 (Median=92 g/wk, N=269) vs Q4 (Median=238 g/wk, N=274)	**CAST Score at 5y, Group differences** Q1 (Ref) vs Q2: B: -0.32, 95% CI: -0.77, 0.13, P>0.05 Q1 (Ref) vs Q3: B: -0.28, 95% CI: -0.72, 0.16, P>0.05 **Q1 (Ref) vs Q4: B: -0.57, 95% CI: -1.01, -0.13, P<0.05** **P trend=0.01**
	Maternal large fatty fish consumption during 1st trimester modeled continuously in 10 g/wk increments (N=1393)	**CAST Score at 5y** **B:-0.02, 95% CI: -0.04, -0.00, P<0.05**

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Julvez, 2016 **Prospective Cohort Study** **INMA; Spain** **(Continued)**	Maternal small fatty fish consumption during 1st trimester in quartiles: Q1 (Ref, Median=0 g/wk, N=668) vs Q2 (Median=37 g/wk, N=235) vs Q3 (Median=69 g/wk, N=240) vs Q4 (Median=147 g/wk, N=250)	**CAST Score at 5y, Group differences** Q1 (Ref) vs Q2: B: -0.19, 95% CI: -0.66, 0.27, P>0.05 Q1 (Ref) vs Q3: B: -0.14, 95% CI: -0.59, 0.31, P>0.05 Q1 (Ref) vs Q4: B: -0.37, 95% CI: -0.81, 0.07, P>0.05 P trend=0.11
	Maternal small fatty fish consumption during 1st trimester modeled continuously in 10 g/wk increments (N=1393)	**CAST Score at 5y** B: -0.00, 95% CI: -0.02, 0.01, P>0.05
	Maternal lean fish consumption during 1st trimester in quintiles: Q1 (Ref, Median=90 g/wk, N=298) vs Q2 (Median=192 g/wk, N=291) vs Q3 (Median=286 g/wk, N=282) vs Q4 (Median=382 g/wk, N=261) vs Q5 (Median=557 g/wk, N=261)	**CAST Score at 5y, Group differences** **Q1 (Ref) vs Q2: B: -0.89, 95% CI: -1.37, -0.41, P<0.05** **Q1 (Ref) vs Q3: B: -0.77, 95% CI: -1.26, -0.28, P<0.05** Q1 (Ref) vs Q4: B: -0.48, 95% CI: -0.98, 0.02, P>0.05 **Q1 (Ref) vs Q5: B: -0.70, 95% CI: -1.22, -0.19, P<0.05** P trend=0.10
	Maternal lean fish consumption during 1st trimester modeled continuously in 10 g/wk increments (N=1393)	**CAST Score at 5y** B: -0.01, 95% CI: -0.02, 0.00, P>0.05
	Maternal shellfish consumption during 1st trimester in quintiles: Q1 (Ref, Median=0 g/wk, N=278) vs Q2 (Median=27 g/wk, N=268) vs Q3 (Median=49 g/wk, N=288) vs Q4 (Median=76 g/wk, N=289) vs Q5 (Median=139 g/wk, N=270)	**CAST Score at 5y, Group differences** Q1 (Ref) vs Q2: B: -0.15, 95% CI: -0.66, 0.36, P>0.05 **Q1 (Ref) vs Q3: B: -0.58, 95% CI: -1.08, -0.09, P<0.05** Q1 (Ref) vs Q4: B: -0.12, 95% CI: -0.61, 0.38, P>0.05 Q1 (Ref) vs Q5: B: -0.05, 95% CI: -0.57, 0.46, P>0.05 P trend=0.92
	Maternal shellfish consumption during 1st trimester modeled continuously in 10 g/wk increments (N=1393)	**CAST Score at 5y** B: 0.01, 95% CI: -0.01, 0.04, P>0.05

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Golding, 2018[6] **Prospective Cohort Study** **ALSPAC; U.K.** ***Summary:*** *Frequency of maternal intake of white fish, oily fish and shellfish was not associated with diagnosed autism by 11y or traits of autism in offspring between the ages of 3y and 11y.*	Maternal intake of oily fish assessed at 32wk gestation: Continuous: 0x/wk, 1x/2wk, > 1x/wk Diagnosed autism: N~1200 Autistic traits: N~8000	*Lower odds ratio of each autistic trait indicates lower likelihood of being in the ~10% of children with worst symptoms.* **Poor sociability (Emotionality, Activity, Sociability temperament scale) at 3y, Linear trend** OR: 0.90, 95% CI: 0.78, 1.04, P=0.15 **Repetitive behavior at 5y, Linear trend** OR: 1.03, 95% CI: 0.92, 1.15, P=0.61 **Poor social cognition (Social and Communication Disorders Checklist) at 7y, Linear trend** OR: 0.98, 95% CI: 0.84, 1.14, P=0.77 **Poor coherence (Children's Communication Checklist coherence scale) at 9y, Linear trend** OR: 1.01, 95% CI: 0.90, 1.14, P=0.85
		Higher odds ratio indicates greater risk of child being diagnosed with autism **Diagnosed autism by 11y, Linear trend** OR: 1.00, 95% CI: 0.68, 1.47, P=0.99
	Maternal intake of shellfish assessed at 32wk gestation: Continuous: 0x/wk, 1x/2wk, > 1x/wk Diagnosed autism: N~1200 Autistic traits: N~8000	**Poor sociability (Emotionality, Activity, Sociability temperament scale) at 3y, Linear trend** OR: 0.91, 95% CI: 0.76, 1.08, P=0.28 **Repetitive behavior at 5y, Linear trend** OR: 1.03, 95% CI: 0.90, 1.17, P=0.71 **Poor social cognition (Social and Communication Disorders Checklist) at 7y, Linear trend** OR: 0.92, 95% CI: 0.77, 1.11, P=0.40 **Poor coherence (Children's Communication Checklist coherence scale) at 9y, Linear trend** OR: 0.94, 95% CI: 0.81, 1.08, P=0.35
		Diagnosed autism by 11y, Linear trend OR: 0.86, 95% CI: 0.54, 1.38, P=0.54

Article	Exposure	Outcome and Results (statistically significant results are bolded)
Golding, 2018 **Prospective Cohort Study** **ALSPAC; U.K.** **(Continued)**	Maternal intake of white fish assessed at 32wk gestation: Continuous: 0x/wk, 1x/2wk, > 1x/wk Diagnosed autism: N~1200 Autistic traits: N~8000	**Poor sociability (Emotionality, Activity, Sociability temperament scale) at 3y, Linear trend** OR: 0.93, 95% CI: 0.77, 1.11, P=0.40 **Repetitive behavior at 5y, Linear trend** OR: 1.01, 95% CI: 0.88, 1.16, P=0.89 **Poor social cognition (Social and Communication Disorders Checklist) at 7y, Linear trend** OR: 0.85, 95% CI: 0.71, 1.03, P=0.09 **Poor coherence (Children's Communication Checklist coherence scale) at 9y, Linear trend** OR: 0.90, 95% CI: 0.78, 1.04, P=0.16
		Diagnosed autism by 11y, Linear trend OR: 1.39, 95% CI: 0.80, 2.40, P=0.24
Steenweg-de Graaff, 2016[21] **Prospective Cohort Study** **Generation R; Netherlands** ***Summary:*** *Maternal fish intake during pregnancy was not associated with child autistic traits at 6y.*	Maternal fish intake (per SD) in early pregnancy modeled continuously (N=3,802) 1 SD increase = 13.6 g/d increase in fish intake.	*Lower scores of the Social Responsiveness Scale (SRS) indicate less child impairment and autistic traits* **SRS at 6y** B: -0.000, 95% CI: -0.009, 0.008, P=0.95
	Maternal seafood intake during early pregnancy: No use (Ref, N=319) vs Use (N=3483)	**SRS at 6y, Group difference** No use (Ref) vs Use: B: -0.22, 95% CI: -0.055, 0.010, P=0.18

[viii] 1 oz = 28.3 g

[ix] Abbreviations: B – beta, CI – confidence interval, d – day(s), g – gram(s), NR – not reported, OR – odds ratio, Ref – reference group, RR – risk ratio, SD – standard deviation, SE – standard error, svg – serving(s), THg – total mercury, vs – versus, wk – week(s), x – time(s), y – year(s), %ile -- percentile

Table 4. Risk of bias for observational studies examining seafood intake during pregnancy and neurocognitive development in the child[x,xi]

Prospective Cohort Studies (outcomes listed only if rating differed by outcome)	Confounding	Selection of participants	Classification of exposures	Departures from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Barbone, 2019[26]	Serious	Low	Low	Low	Moderate	Low	Moderate
Daniels, 2004[1]	Serious	Low	Moderate	Low	Low	Low	Moderate
Davidson, 2008[2]	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Deroma, 2013[3]	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Furlong, 2018[4]	Serious	Low	Serious	Moderate	Moderate	Low	Moderate
Gale, 2008[5]	Serious	Low	Moderate	No information	Low	Low	Moderate
Golding, 2018[6]	Serious	No information	Moderate	No information	No information	Low	Moderate
Hibbeln, 2007[7]	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Moderate
Hisada, 2017[8]	Serious	Low	Serious	Low	No information	Moderate	Moderate
Hu, 2016[9]	Serious	Low	Serious	No information	Moderate	Low	Moderate
Julvez, 2016[10] (Developmental domains)	Moderate	Low	Low	Low	Moderate	Low	Serious
Julvez, 2016[10] (ASD)	Serious	Low	Low	Low	Moderate	Low	Serious
Lederman, 2008[11]	Serious	Low	Serious	No information	Moderate	Low	Moderate
Llop, 2012[12]	Serious	Low	Low	Low	No information	Low	Moderate
Mendez, 2009[13]	Serious	Moderate	Moderate	Low	Low	Low	Moderate
Mesirow, 2017[14]	Critical	Serious	Moderate	Low	Low	Moderate	Moderate
Normia, 2019[15]	Serious	Low	Serious	No information	No information	Low	Moderate
Oken, 2005[19]	Serious	Low	Low	Low	No information	Low	Moderate

[x] A detailed description of the methodology used for assessing risk of bias is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

[xi] Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

Prospective Cohort Studies (outcomes listed only if rating differed by outcome)	Confounding	Selection of participants	Classification of exposures	Departures from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Oken, 2008b[16]	Serious	Low	Low	Low	Moderate	Low	Moderate
Oken, 2008a[17]	Serious	Low	Low	Low	Moderate	Low	Moderate
Oken, 2016[18]	Serious	Low	Moderate	Low	Low	Low	Moderate
Sagiv, 2012[20]	Serious	Low	Moderate	Low	Moderate	Moderate	Moderate
Steenweg-de Graaff, 2016[21]	Serious	Low	Low	Low	Moderate	Moderate	Moderate
Valent, 2013[22]	Serious	Low	Low	Low	Moderate	Low	Moderate
Vejrup, 2018[23]	Serious	Low	Low	Low	Serious	Moderate	Moderate
Williams, 2001[24]	Serious	Low	Moderate	Moderate	Low	Low	Moderate
Xu, 2016[25]	Serious	Low	Serious	No information	Low	Low	Moderate

METHODOLOGY

The NESR team used its rigorous, protocol-driven methodology to support the 2020 Dietary Guidelines Advisory Committee in conducting this systematic review.

NESR's systematic review methodology involves:

- Developing a protocol,
- Searching for and selecting studies,
- Extracting data from and assessing the risk of bias of each included study,
- Synthesizing the evidence,
- Developing conclusion statements,
- Grading the evidence underlying the conclusion statements, and
- Recommending future research.

A detailed description of the methodology used in conducting this systematic review is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews, and can be found in the 2020 Dietary Guidelines Advisory Committee Report, Part C: Methodology.[xii] This systematic review was peer reviewed by Federal scientists, and information about the peer review process can also be found in the Committee's Report, Part C. Methodology. Additional information about this systematic review, including a description of and rationale for any modifications made to the protocol can be found in the 2020 Dietary Guidelines Advisory Committee Report, Part D: Chapter 9. Dietary Fats and Seafood.

Below are details of the final protocol for the systematic review described herein, including the:

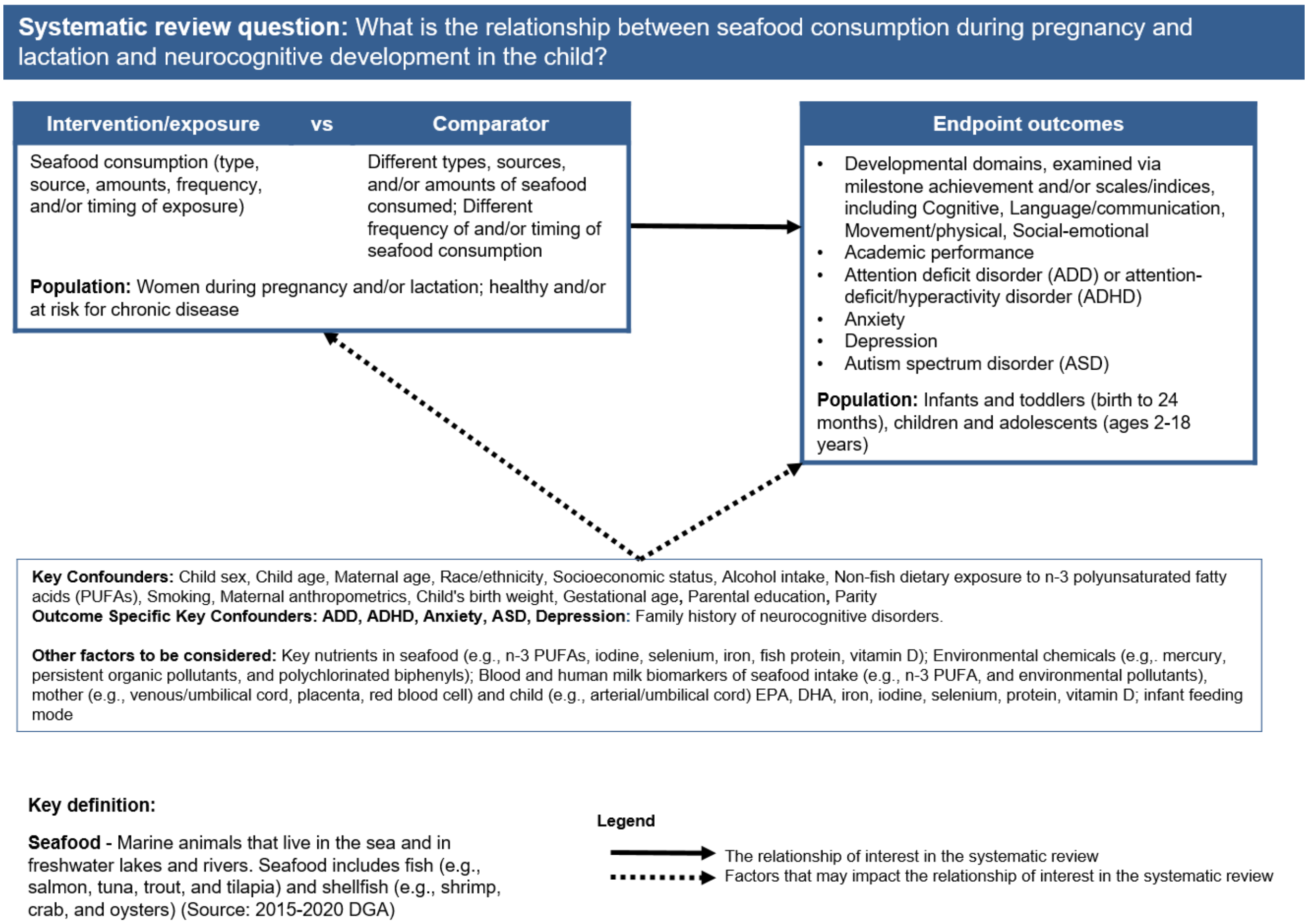
- Analytic framework
- Literature search and screening plan
- Literature search and screening results

[xii] Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

ANALYTIC FRAMEWORK

The analytic framework (**Figure 1**) illustrates the overall scope of the systematic review, including the population, the interventions and/or exposures, comparators, and outcomes of interest. It also includes definitions of key terms and identifies key confounders considered in the systematic review. The inclusion and exclusion criteria that follow provide additional information about how parts of the analytic framework were defined and operationalized for the review.

Figure 1: Analytic framework



LITERATURE SEARCH AND SCREENING PLAN

Inclusion and exclusion criteria

This table (**Table 5**) provides the inclusion and exclusion criteria for the systematic review. The inclusion and exclusion criteria are a set of characteristics used to determine which articles identified in the literature search were included in or excluded from the systematic review.

Table 5. Inclusion and exclusion criteria

<table>
<tr><th>Category</th><th>Inclusion Criteria</th><th>Exclusion Criteria</th></tr>
<tr><td>Study design</td><td>• Randomized controlled trials
• Non-randomized controlled trials, including quasi-experimental and controlled before-and-after studies
• Prospective cohort studies
• Retrospective cohort studies
• Nested case-control studies</td><td>• Uncontrolled trials
• Case-control studies
• Cross-sectional studies
• Uncontrolled before-and-after studies
• Narrative reviews
• Systematic reviews
• Meta-analyses</td></tr>
<tr><td>Intervention/ exposure</td><td>• Seafood consumption measured prior to outcome assessment
○ Type (e.g., salmon, tuna bass)
○ Source (e.g., sea fresh water, farmed, wild)
○ Amount/frequency of intake
○ Timing of exposure (e.g., age at intake)
• Dietary intake (e.g., from food frequency questionnaires, dietary recall, fish/seafood screeners) may be validated with biomarkers for PUFA or MeHg, but not substituted.</td><td>• No measure of seafood consumption (i.e., studies that only examined biomarkers for consumption)
• n-3 supplement studies which do not evaluate seafood consumption
• Studies evaluating infant formula with added DHA and/or EPA</td></tr>
<tr><td>Comparator</td><td>• Different types, sources, amounts, frequency, and/or timing of exposure of seafood consumption</td><td>• No comparator</td></tr>
</table>

Category	Inclusion Criteria	Exclusion Criteria
Outcomes	• Developmental milestones, including neurocognitive development o Developmental domains examined via milestone achievement and/or scales/indices, including: ▪ cognitive, ▪ language/communication, ▪ movement/physical, ▪ social/emotional • Academic performance • Attention deficit disorder (ADD) or attention-deficit/hyperactivity disorder (ADHD) • Anxiety • Depression • Autism spectrum disorder (ASD)	• No measure of neurocognitive development
Date of publication	• January 2000 to October 2019	• Articles published prior to January 2000 or after October 2019
Publication status	• Articles that have been peer-reviewed	• Articles that have not been peer-reviewed and are not published in peer-reviewed journals, including conference proceedings unpublished data manuscripts, reports, and abstracts
Language of publication	• Articles published in English	• Articles published in languages other than English
Country[xiii]	• Studies conducted in countries ranked as high or very high human development	• Studies conducted in countries ranked as medium or lower human development

Category	Inclusion Criteria	Exclusion Criteria

Study participants	• Human participants
	• At intervention/exposure
	  ○ Females who are pregnant and/or lactating
	• At outcome
	  ○ Males and females
		• Non-human subjects (e.g., animal models or in-vitro models)

Age of study participants	• Age at outcome:
	  ○ Infants/toddlers (0-24 months)
	  ○ Children/adolescents (2-18 years)
		• Age at outcome:
		  ○ Adults (ages 19-64 years)
		  ○ Older adults (ages 65 years and older)

Health status of study participants	• Studies that enroll participants who are healthy and/or at risk for chronic disease, including those with obesity • Studies that enroll **some** participants diagnosed with a disease or with the neurocognitive development and/or health outcomes of interest • Studies that enroll infants born full-term (≥37 weeks and 0/7 days gestational age) • Studies that enroll **some** infants born preterm (gestational age <37 weeks and 0/7 days), infants with low birth weight (<2500g), and/or infants born small for gestational age	• Studies that **exclusively** enroll participants diagnosed with a disease or hospitalized with an illness or injury. (For this criterion, studies that exclusively enroll participants with obesity will not be excluded.) • Studies that **exclusively** enroll participants with the neurocognitive development and/or health outcomes of interest • Studies that **exclusively** enroll infants born preterm (gestational age <37 weeks and 0/7 days), infants with low birth weight (<2500g), and/or infants born small for gestational age

[xiii] The Human Development classification was based on the Human Development Index (HDI) ranking from the year the study intervention occurred or data were collected (UN Development Program. HDI 1990-2017 HDRO calculations based on data from UNDESA (2017a), UNESCO Institute for Statistics (2018), United Nations Statistics Division (2018b), World Bank (2018b), Barro and Lee (2016) and IMF (2018). Available from: http://hdr.undp.org/en/data). If the study did not report the year in which the intervention occurred or data were collected, the HDI classification for the year of publication was applied. HDI values are available from 1980, and then from 1990 to present. If a study was conducted prior to 1990, the HDI classification from 1990 was applied. When a country was not included in the HDI ranking, the current country classification from the World Bank was used instead (The World Bank. World Bank country and lending group) Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world- country-and-lending-groups).

Electronic databases and search terms

Listed below are the databases and search terms searched to identify all potentially relevant articles that have been published to address this systematic review question and a second systematic review question on seafood intake during childhood and adolescence and neurocognitive development.

PubMed

- Provider: U.S. National Library of Medicine
- Date(s) Searched: October 23, 2019
- Date range searched: January 1, 2000 - October 23, 2019
- Search Terms:

#1 - "Pregnancy"[Mesh] OR pregnancy OR "Pregnant Women"[Mesh] OR "pregnant women" OR pregnant OR "Lactation"[Mesh] OR lactation OR "Breast Feeding"[Mesh] OR "breast feeding" OR "Maternal Health"[Mesh] OR "maternal health" OR "Prenatal Exposure Delayed Effects"[Mesh] OR "Maternal Exposure"[Mesh] OR pregnan*[tiab] OR pre-pregnancy[tiab] OR prenatal[tiab] OR maternal OR mother* OR postpartum OR perinatal OR peri-natal OR pre-conception OR preconception OR peri-conception OR periconceptional OR "Peripartum Period"[Mesh] OR peripartum[tiab] OR peri-partum[tiab] OR gestation* OR natal OR puerperium[tiab] OR "Maternal Nutritional Physiological Phenomena"[Mesh] OR "Infant"[Mesh] OR infant OR "Infant, Newborn"[Mesh] OR newborn OR baby OR babies OR "Fetus"[Mesh] OR fetus OR "Child"[Mesh] OR toddler* OR child OR children OR childhood OR "Child, Preschool"[Mesh] OR preschool OR teen* OR "Adolescent"[Mesh] OR adolescent* OR "Pediatrics"[Mesh] OR pediatric*

#2 - Seafood OR "Seafood"[Mesh] OR seafoods OR sea-food OR “sea food” OR sea-foods OR fish OR “fish consumption” OR "Fishes"[Mesh] OR fishes OR "Fish Proteins"[Mesh] OR “fish proteins” OR “fish products” OR “fish flour” OR “fatty fish” OR shellfish OR “shellfish proteins” OR “mercury poisoning” OR "Mercury Poisoning"[Mesh] OR methylmercury OR "Sharks"[Mesh] OR sharks OR swordfish OR "Tuna"[Mesh] OR tuna OR "Salmon"[Mesh] OR salmon OR sardines OR "Gadiformes"[Mesh] OR pollock OR "Flounder"[Mesh] OR flounder OR cod OR "Tilapia"[Mesh] OR tilapia OR shrimp OR "Ostreidae"[Mesh] OR oysters OR "Mya"[Mesh] OR "Bivalvia"[Mesh] OR clams OR "Pectinidae"[Mesh] OR scallops OR "Brachyura"[Mesh] OR crab OR "Perciformes"[Mesh] OR mackerel OR “Catfishes"[Mesh] OR catfishes OR "Trout"[Mesh] OR trout OR lobster OR "Decapodiformes"[Mesh] OR squid OR halibut OR “mahi mahi” OR crawfish OR anchov* OR herring OR rockfish OR marine product* OR "Fatty Acids, Omega-3"[Mesh]

#3 - "Mental Disorders"[Mesh] OR mental disorder*[tiab] OR "Cognition"[Mesh] OR cognition[tiab] OR cognitive[tiab] OR metacognition[tiab] OR neurocognitive[tiab] OR neurodevelop*[tiab] OR neurological[tiab] OR "Depression"[Mesh] OR depression[tiab] OR Alzheimer*[tiab] OR senility[tiab] OR senile[tiab] OR presenile[tiab] OR "Dementia"[Mesh] OR dementia[tiab] OR anxiety[tiab] OR "Psychomotor Performance"[Mesh] OR motor skill*[tiab] OR "Executive Function"[Mesh] OR executive function* OR attention deficit disorder*[tiab] OR ADHD[tiab] OR "Child Behavior Disorders"[Mesh] OR developmental disorder*[tiab] OR "Autism Spectrum Disorder"[Mesh] OR Autism[tiab] OR Asperger[tiab] OR language processing[tiab] OR language delay* OR "Child Development"[Mesh] OR child develop*[tiab] OR developmental delay[tiab] OR developmental disabilit*[tiab] OR motor skill*[tiab] OR "Problem Solving"[Mesh] OR developmental domain* OR academic performance[tiab] Or academic achievement[tiab] OR academic failure[tiab] OR academic success*[tiab] OR "Mental Health"[Mesh] OR mental health[tiab] OR "Mental Processes"[Mesh:NoExp]

#4 - (#1 AND #2 AND #3)

#5 - (#1 AND #2 AND #3) NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])) NOT (editorial[ptyp] OR comment[ptyp] OR news[ptyp] OR letter[ptyp] OR review[ptyp] OR systematic review[ptyp] OR systematic review[ti] OR meta-analysis[ptyp] OR meta-analysis[ti] OR meta-analyses[ti] OR retracted publication[ptyp] OR retraction of publication[ptyp] OR retraction of publication[tiab] OR retraction notice[ti]) Filters: Publication date from 2000/01/01 to 2019/10/23; English

Cochrane Central Register of Controlled Trials (CENTRAL)

- Provider: John Wiley & Sons
- Date(s) Searched: October 23, 2019
- Date range searched: January 1, 2000 - October 23, 2019
- Search Terms:

#1 - [mh "Pregnancy"] OR [mh "Pregnant Women"] OR [mh "Lactation"] OR [mh "Breast Feeding"] OR [mh "Maternal Health"] OR [mh "Prenatal Exposure Delayed Effects"] OR [mh "Maternal Exposure"] OR [mh "Peripartum Period"] OR [mh "Maternal Nutritional Physiological Phenomena"] OR [mh Infant] OR [mh "Infant, Newborn"] OR [mh Fetus] OR [mh Child] OR [mh "Child, Preschool"] OR [mh "Adolescent"] OR [mh "Pediatrics"]

#2 - (pregnan* OR lactation OR "breast feeding" OR "maternal health" OR pre-pregnancy OR prenatal OR maternal OR mother* OR postpartum OR perinatal OR peri-natal OR pre-conception OR preconception OR peri-conception OR periconceptional OR peripartum OR peri-partum OR gestation* OR natal OR puerperium OR infant OR newborn OR baby OR babies OR fetus OR toddler* OR child OR children OR childhood OR preschool OR teen* OR adolescent* OR pediatric*):ti,ab,kw

#3 - #1 OR #2

#4 - [mh "Seafood"] OR [mh "Fishes"] OR [mh "Fish Proteins"] OR [mh "Mercury Poisoning"] OR [mh "Sharks"] OR [mh "Tuna"] OR [mh "Salmon"] OR [mh "Gadiformes"] OR [mh "Flounder"] OR [mh "Tilapia"] OR [mh "Ostreidae"] OR [mh "Mya"] OR [mh "Bivalvia"] OR [mh "Pectinidae"] OR [mh "Brachyura"] OR [mh "Perciformes"] OR [mh "Catfishes"] OR [mh "Trout"] OR [mh "Decapodiformes"] OR [mh "Fatty Acids, Omega-3"]

#5 - (seafood OR seafoods OR sea-food OR “sea food” OR sea-foods OR fish OR “fish consumption” OR fishes OR “fish proteins” OR “fish products” OR “fish flour” OR “fatty fish” OR shellfish OR “shellfish proteins” OR methylmercury OR “mercury poisoning” OR sharks OR swordfish OR tuna OR salmon OR sardines OR pollock OR flounder OR cod OR tilapia OR shrimp OR oysters OR clams OR scallops OR crab OR mackerel OR catfishes OR trout OR lobster OR squid OR halibut OR “mahi mahi” OR crawfish OR anchov* OR herring OR rockfish OR marine product*):ti,ab,kw

#6 - #4 OR #5

#7 - [mh "Mental Disorders"] OR [mh "Cognition"] OR [mh "Depression"] OR [mh "Dementia"] OR [mh "Psychomotor Performance"] OR [mh "Executive Function"] OR [mh "Child Behavior Disorders"] OR [mh "Autism Spectrum Disorder"] OR [mh "Child Development"] OR [mh

"Problem Solving"] OR [mh "Mental Health"] OR [mh ^"Mental Processes"]

#8 - (“mental disorder*” OR cognition OR cognitive OR metacognition OR neurocognitive OR neurodevelop* OR neurological OR depression OR Alzheimer* OR senility OR senile OR presenile OR dementia OR anxiety OR motor skill* OR “attention deficit disorder*” OR ADHD OR “developmental disorder*” OR Autism OR Asperger OR “language processing” OR “language delay*” OR “child develop*” OR “developmental delay” OR “developmental disabilit*” OR “motor skill*” OR “developmental domain*” OR “academic performance” OR “academic achievement” OR “academic failure” OR “academic success*” OR “mental health”):ti,ab,kw

#9 - #7 OR #8

#10 - #3 AND #6 AND #9" with Publication Year from 2000 to 2019, in Trials (Word variations have been searched)

Embase

- Provider: Elsevier
- Date(s) Searched: October 23, 2019
- Date range searched: January 1, 2000 - October 23, 2019
- Search Terms:

#1 - 'pregnancy'/exp OR 'pregnant woman'/exp OR 'lactation'/exp OR 'breast feeding'/exp OR 'maternal welfare'/exp OR 'prenatal exposure'/exp OR 'mother'/exp OR 'perinatal period'/exp OR 'maternal nutrition'/exp OR 'infant'/exp OR 'newborn'/exp OR 'baby'/exp OR 'fetus'/exp OR 'child'/exp OR 'childhood'/exp OR 'preschool'/exp OR 'adolescent'/exp OR 'pediatrics'/exp

#2 - pregnan*:ab,ti OR lactation:ab,ti OR 'breast feeding':ab,ti OR 'prenatal exposure':ab,ti OR 'pre pregnancy':ab,ti OR prenatal:ab,ti OR maternal:ab,ti OR mother*:ab,ti OR postpartum:ab,ti OR perinatal:ab,ti OR 'peri natal':ab,ti OR 'pre conception':ab,ti OR preconception:ab,ti OR 'peri conception':ab,ti OR periconceptional:ab,ti OR peripartum:ab,ti OR gestation*:ab,ti OR natal:ab,ti OR puerperium:ab,ti OR infant:ab,ti OR newborn*:ab,ti OR childhood:ab,ti OR baby:ab,ti OR babies:ab,ti OR fetus:ab,ti OR child:ab,ti OR preschool:ab,ti OR adolescent:ab,ti OR teen*:ab,ti OR pediatric*:ab,ti

#3 - #1 OR #2

#4 - 'sea food'/exp OR 'fish'/exp OR 'fish consumption'/exp OR 'fish protein'/exp OR 'fish product'/exp OR 'fish meal'/exp OR 'fatty fish'/exp OR 'shellfish'/exp OR 'shellfish protein'/exp OR 'mercurialism'/exp OR 'methylmercury'/exp OR 'shark'/exp OR 'swordfish'/exp OR 'tuna'/exp OR 'salmonine'/exp OR 'sardine'/exp OR 'gadiformes'/exp OR 'flounder'/exp OR 'atlantic cod'/exp OR 'tilapia'/exp OR 'shrimp'/exp OR 'oyster'/exp OR 'mya'/exp OR 'bivalve'/exp OR 'clam'/exp OR 'scallop'/exp OR 'brachyura'/exp OR 'crab'/exp OR 'perciformes'/exp OR 'mackerel'/exp OR 'catfish'/exp OR 'lobster'/exp OR 'decapodiformes'/exp OR 'squid'/exp OR 'halibut'/exp OR 'crayfish'/exp OR 'anchovy'/exp OR 'herring'/exp OR 'rockfish'/exp OR 'omega 3 fatty acid'/exp

#5 - seafood*:ab,ti OR fish:ab,ti OR 'fish consumption':ab,ti OR 'fish protein*':ab,ti OR 'fish product*':ab,ti OR 'fish meal*':ab,ti OR 'fatty fish':ab,ti OR 'shellfish protein*':ab,ti OR mercurialism:ab,ti OR methylmercury:ab,ti OR shark:ab,ti OR swordfish:ab,ti OR tuna:ab,ti OR salmonine:ab,ti OR salmon:ab,ti OR sardine*:ab,ti OR gadiformes:ab,ti OR pollock:ab,ti OR flounder:ab,ti OR cod:ab,ti OR tilapia:ab,ti OR shrimp:ab,ti OR oyster*:ab,ti OR bivalve:ab,ti OR mya:ab,ti OR clam:ab,ti OR clams:ab,ti OR scallop*:ab,ti OR crab:ab,ti OR perciformes:ab,ti OR mackerel:ab,ti OR catfish:ab,ti OR trout:ab,ti OR lobster:ab,ti OR squid:ab,ti OR decapodiformes:ab,ti OR halibut:ab,ti OR 'mahi mahi':ab,ti OR crayfish:ab,ti OR crawfish:ab,ti OR achov*:ab,ti OR herring:ab,ti OR rockfish:ab,ti OR 'marine product*':ab,ti OR 'omega 3 fatty acid*':ab,ti

#6 - #4 OR #5

#7 - 'mental disease'/exp OR 'cognition'/exp OR 'depression'/exp OR 'dementia'/exp OR 'anxiety'/exp OR 'psychomotor performance'/exp OR 'executive function'/exp OR 'child development'/exp OR 'developmental disorder'/exp OR 'psychomotor disorder'/exp OR 'problem solving'/exp OR 'mental health'/exp OR 'mental function'/de

#8 - 'mental disorder*':ab,ti OR cognition:ab,ti OR cognitive:ab,ti OR metacognition:ab,ti OR neurocognitive:ab,ti OR neurodevelop*:ab,ti OR neurological:ab,ti OR depression:ab,ti OR alzheimer*:ab,ti OR senility:ab,ti OR senile:ab,ti OR presenile:ab,ti OR dementia:ab,ti OR anxiety:ab,ti OR 'motor skill*':ab,ti OR 'executive function':ab,ti OR 'attention deficit disorder':ab,ti OR adhd:ab,ti OR 'developmental disorder':ab,ti OR 'language processing':ab,ti OR 'language delay*':ab,ti OR 'child develop*':ab,ti OR autism:ab,ti OR asperger:ab,ti OR 'developmental delay':ab,ti OR 'developmental disabilit*or developmental domain*':ab,ti OR 'academic performance':ab,ti OR 'academic achievement':ab,ti OR 'academic failure':ab,ti OR 'academic success*':ab,ti OR 'mental health':ab,ti

#9 - #7 OR #8

#10 - #3 AND #6 AND #9

#11 - #3 AND #6 AND #9 AND ([article]/lim OR [article in press]/lim) AND [humans]/lim AND [english]/lim AND [2000-2019]/py NOT ([conference abstract]/lim OR [conference review]/lim OR [conference paper]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [systematic review]/lim OR [meta analysis]/lim)

Cumulative Index of Nursing and Allied Health Literature (CINAHL Plus)

- Provider: EBSCO*host*
- Date(s) Searched: October 23, 2019
- Date range searched: January 1, 2000 - October 23, 2019
- Search Terms:

*#**S1 -*** (MH "Pregnancy") OR pregnancy OR (MH "Expectant Mothers") OR “expected mothers” OR pregnant OR (MH "Lactation") OR lactation OR (MH "Breast Feeding") OR breastfeeding OR (MH "Maternal-Child Health") OR “maternal child health” OR (MH "Prenatal Exposure Delayed Effects") OR (MH "Maternal Exposure") OR pregnan* OR pre-pregnancy OR prenatal OR maternal OR mother OR postpartum OR perinatal OR perinatal OR pre-conception OR preconception OR peri-conception OR periconceptional OR "peripartum period" OR peripartum OR peri-partum OR gestation* OR natal OR (MH "Puerperium") OR Puerperium OR (MH "Maternal Nutritional Physiology") OR (MH "Infant") OR infant OR (MH "Infant, Newborn") OR newborn OR baby OR babies OR (MH "Fetus") OR fetus OR (MH "Child") OR child OR (MH "Child, Preschool") OR toddler OR (MH "Adolescence") OR teen* OR adolescent OR (MH "Pediatrics") OR pediatrics

*#**S2 -*** seafood OR (MH "Seafood") OR seafood* OR sea-food OR “sea food” OR (MH "Fish") OR fish OR "fish consumption" OR fishes OR “fish protein*” OR “fish product*” OR “fish flour”

OR “fatty fish” OR (MH "Shellfish") OR shellfish OR “shellfish proteins” OR “mercury poisoning” OR (MH "Mercury Poisoning") OR methylmercury OR shark* OR swordfish OR tuna OR salmon OR sardine* OR Pollock OR flounder OR cod OR tilapia OR shrimp OR oyster* OR clams OR scallops OR crab OR mackerel OR catfish* OR trout OR lobster* OR squid OR halibut OR “mahi mahi” OR crawfish OR achov* OR herring OR rockfish OR marine product* OR (MH "Fatty Acids, Omega-3")

#S3 - (MH "Mental Disorders") OR mental disorder* OR (MH "Cognition") OR cognition OR cognitive OR metacognition OR neurocognitive OR neurodevelop* OR neurological OR “cognitive dysfunction” OR “depressive disorders OR (MH "Depression") OR depression OR (MH "Alzheimer's Disease") OR “Alzheimer’s disease” OR (MH "Dementia, Senile") OR senile OR senility OR presenile OR (MH "Dementia") OR (MH "Anxiety") OR anxiety OR (MH "Psychomotor Performance") OR motor skill* OR (MH "Executive Function") OR executive function* OR (MH "Attention Deficit Hyperactivity Disorder") OR attention deficit disorder* OR ADHD OR (MH "Child Behavior Disorders") OR developmental disorder* OR (MH "Autistic Disorder") OR autism OR Asperger OR “language processing” OR language delay* OR (MH "Child Development") OR child develop* OR (MH "Developmental Disabilities") OR developmental delay* OR developmental disabilit* OR (MH "Motor Skills Disorders") OR motor skill* OR (MH "Problem Solving") OR developmental domain* OR “academic performance” OR “academic achievement” OR “academic failure” OR academic success* OR (MH "Mental Health") OR "mental health" OR (MH "Mental Processes")

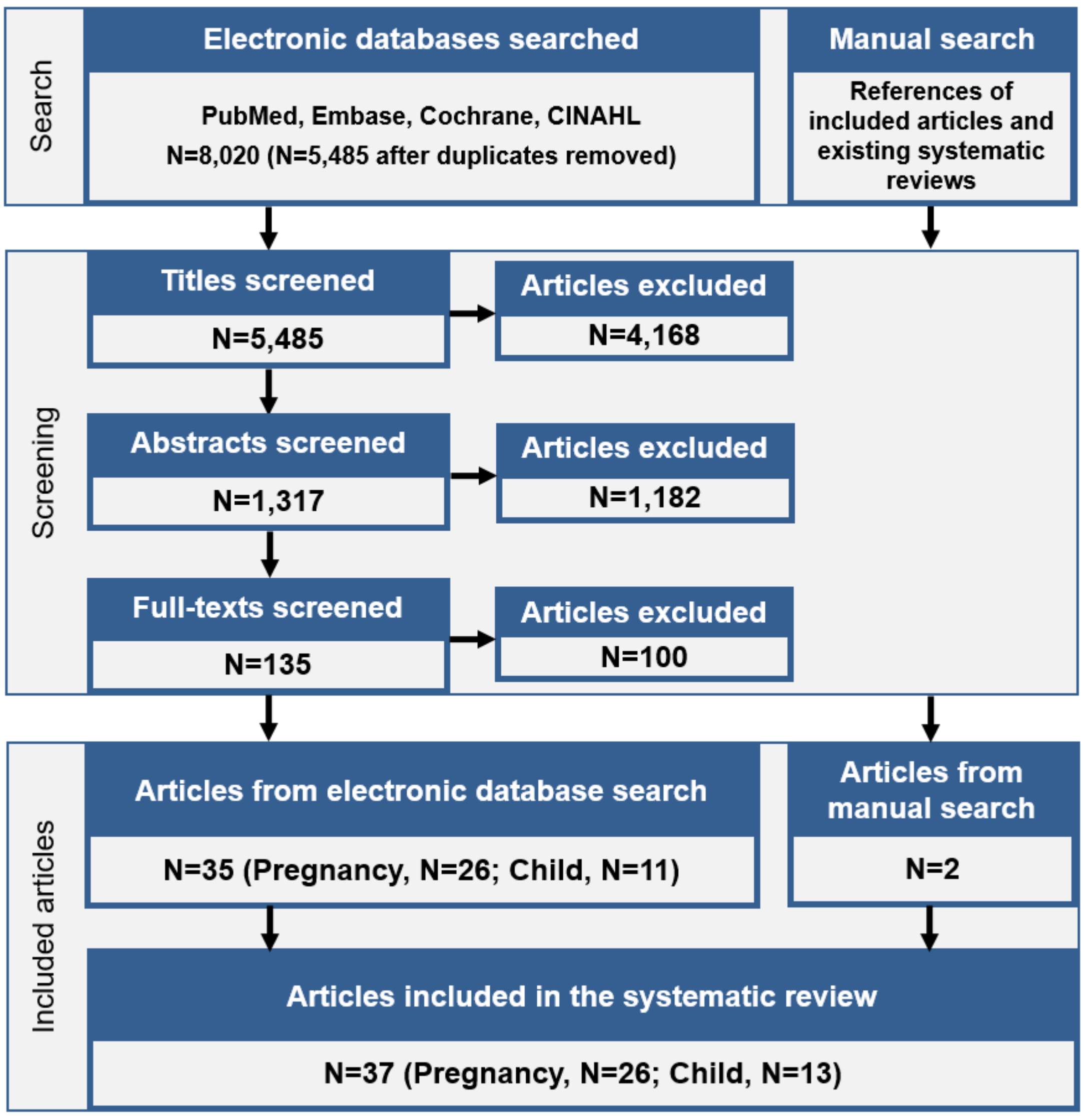
#S4 - S1 AND S2 AND S3

#S5 - S1 AND S2 AND S3 NOT (MH "Literature Review" OR MH "Meta Analysis" OR MH "Systematic Review" OR MH "News" OR MH "Retracted Publication" OR MH "Retraction of Publication") Limiters - Publication Year: 2000-2019; Peer Reviewed; English Language; Human

LITERATURE SEARCH AND SCREENING RESULTS

The flow chart (**Figure 2**) below illustrates the literature search and screening results for articles examining this systematic review question and a second question on seafood consumption during childhood and adolescence and neurocognitive development. The results of the electronic database searches, after removal of duplicates, were screened independently by two NESR analysts using a step-wise process by reviewing titles, abstracts, and full-texts to determine which articles met the inclusion criteria. Refer to **Table 6** for the rationale for exclusion for each excluded full-text article. A manual search was done to find articles that were not identified when searching the electronic databases; all manually identified articles are also screened to determine whether they meet criteria for inclusion.

Figure 2: Flow chart of literature search and screening results[xiv]



[xiv] Two articles were included in both the review for pregnancy and lactation and the review for childhood and adolescence

Excluded articles

The table below lists the articles excluded after full-text screening for this systematic review question and a second question on seafood consumption during childhood and adolescence and neurocognitive development, and includes columns for the categories of inclusion and exclusion criteria (see **Table 5**) that studies were excluded based on. At least one reason for exclusion is provided for each article, as indicated by an "X" in one of the columns, though this may not reflect all possible reasons for exclusion. Information about articles excluded after title and abstract screening is available upon request.

Table 6. Articles excluded after full-text screening with rationale for exclusion

	Citation	Intervention/ Exposure	Age	Outcome	Study Design	Comparator	Publication Status
1.	Al-Ghannami SS, Al-Adawi S, Ghebremeskel K, et al. Randomized open-label trial of docosahexaenoic acid-enriched fish oil and fish meal on cognitive and behavioral functioning in Omani children. *Nutrition.* 2019;57:167-172. doi:10.1016/j.nut.2018.04.008.					X	
2.	Andrew MJ, Parr JR, Montague-Johnson C, et al. Nutritional intervention and neurodevelopmental outcome in infants with suspected cerebral palsy: the Dolphin infant double-blind randomized controlled trial. *Dev Med Child Neurol.* 2018;60(9):906-913. doi:10.1111/dmcn.13586.	X					
3.	Boucher O, Muckle G, Ayotte P, Dewailly E, Jacobson SW, Jacobson JL. Altered fine motor function at school age in Inuit children exposed to PCBs, methylmercury, and lead. *Environ Int.* 2016;95:144-51. doi:10.1016/j.envint.2016.08.010.	X					
4.	Braarud HC, Markhus MW, Skotheim S, et al. Maternal DHA Status during Pregnancy Has a Positive Impact on Infant Problem Solving: A Norwegian Prospective Observation Study. *Nutrients.* 2018;10(5). pii: E529. doi:10.3390/nu10050529.	X					

	Citation	Intervention/ Exposure	Age	Outcome	Study Design	Comparator	Publication Status
5.	Brouwer-Brolsma EM, van de Rest O, Godschalk R, Zeegers MPA, Gielen M, de Groot RHM. Associations between maternal long-chain polyunsaturated fatty acid concentrations and child cognition at 7 years of age: The MEFAB birth cohort. *Prostaglandins Leukot Essent Fatty Acids.* 2017;126:92-97. doi:10.1016/j.plefa.2017.09.012.	X					
6.	Budtz-Jorgensen E, Grandjean P, Weihe P. Separation of risks and benefits of seafood intake. *Environ Health Perspect.* 2007;115(3):323-7. doi:10.1289/ehp.9738.				X		
7.	Butler LJ, Janulewicz PA, Carwile JL, White RF, Winter MR, Aschengrau A. Childhood and adolescent fish consumption and adult neuropsychological performance: An analysis from the Cape Cod Health Study. *Neurotoxicol Teratol*. 2017;61:47-57. doi:10.1016/j.ntt.2017.03.001.				X		
8.	Carwile JL, Butler LJ, Janulewicz PA, Winter MR, Aschengrau A. Childhood Fish Consumption and Learning and Behavioral Disorders. *Int J Environ Res Public Health*. 2016;13(11):1069. doi:10.3390/ijerph13111069				X		
9.	Chen MYY, Wong, WWK, et al. Quantitative risk-benefit analysis of fish consumption for women of child-bearing age in Hong Kong. *Food Addit Contam Part A Chem Anal Control Exp Risk Assess.* 2014;31(1):48-53. doi:10.1080/19440049.2013.855947.			X			
10.	Chien LC, Gao CS, Lin HH. Hair mercury concentration and fish consumption, Risk and perceptions of risk among women of childbearing age. *Environ Res.* 2010;110(1):123-129. doi:10.1016/j.envres.2009.10.001.			X	X		
11.	Choi AL, Mogensen UB, Bjerve KS, et al. Negative confounding by essential fatty acids in methylmercury neurotoxicity associations. *Neurotoxicol Teratol.* 2014;42,85-92. doi:10.1016/j.ntt.2014.02.003.	X					

	Citation	Intervention/ Exposure	Age	Outcome	Study Design	Comparator	Publication Status
12.	Davidson PW, Cory-Slechta DA, Thurston SW, et al. Fish consumption and prenatal methylmercury exposure, cognitive and behavioral outcomes in the main cohort at 17 years from the Seychelles child development study. *Neurotoxicology.* 2011;32(6):711-7. doi:10.1016/j.neuro.2011.08.003.	X	X				
13.	Davidson PW, Kost J, Myers GJ, Cox C, Clarkson TW, Shamlaye, C. F. Methylmercury and neurodevelopment, reanalysis of the Seychelles Child Development Study outcomes at 66 months of age. *JAMA.* 2001;285(10):1291-3. doi:10.1001/jama.285.10.1291.				X		
14.	Davidson PW, Leste A, Benstrong E, et al. Fish consumption, mercury exposure, and their associations with scholastic achievement in the Seychelles Child Development Study. *Neurotoxicology.* 2010;31(5):439-47. doi:10.1016/j.neuro.2010.05.010.	X					
15.	de Groot RH, Ouwehand C, Jolles J. Eating the right amount of fish, inverted U-shape association between fish consumption and cognitive performance and academic achievement in Dutch adolescents. *Prostaglandins Leukot Essent Fatty Acids.* 2012;86(3):113-7. doi:10.1016/j.plefa.2012.01.002.				X		
16.	Debes F, Budtz-Jorgensen E, Weihe P, White RF, Grandjean P. Impact of prenatal methylmercury exposure on neurobehavioral function at age 14 years. *Neurotoxicol Teratol.* 2006;28(5):536-47. doi:10.1016/j.ntt.2006.02.005.	X					
17.	Debes F, Weihe P, Grandjean P. Cognitive deficits at age 22 years associated with prenatal exposure to methylmercury. *Cortex.* 2016;74,358-69. doi:10.1016/j.cortex.2015.05.017.	X	X				

	Citation	Intervention/ Exposure	Age	Outcome	Study Design	Comparator	Publication Status
18.	Dorea JG, Marques RC, Abreu L. Milestone achievement and neurodevelopment of rural Amazonian toddlers (12 to 24 months) with different methylmercury and ethylmercury exposure. *J Toxicol Environ Health A.* 2014;77:1-13. doi:10.1080/15287394.2014.861335.	X			X		
19.	Dye D. Mother's omega-3 fatty acid deficit impairs infant's neurological development. *Life Extension.* 2008;14:28-28.						X
20.	Emmett PM. Dietary Patterns during Complementary Feeding and Later Outcomes. *Nestle Nutr Inst Workshop Ser.* 2016;85:145-54. doi:10.1159/000439505.	X			X		
21.	Emmett PM, Jones LR, Golding J. Pregnancy diet and associated outcomes in the Avon Longitudinal Study of Parents and Children. *Nutr Rev.* 2015;73(Suppl 3):154-74. doi:10.1093/nutrit/nuv053.				X		
22.	Freire C, Ramos R, Lopez-Espinosa MJ, et al.. Hair mercury levels, fish consumption, and cognitive development in preschool children from Granada Spain. *Environ Res.* 2010;110(1):96-104. doi:10.1016/j.envres.2009.10.005.	X			X		
23.	Gao L, Cui SS, Han Y, Dai W, Su YY, Zhang X. Does periconceptional fish consumption by parents affect the incidence of Autism Spectrum Disorder and intelligence deficiency? A case-control study in Tianjin, China. *Biomed Environ Sci.* 2016;29(12):885-892. doi:10.3967/bes2016.118.				X		
24.	Gao L, Xi QQ, Wu J, et al. Association between prenatal environmental factors and child Autism: A case control study in Tianjin, China. *Biomed Environ Sci.* 2015;28(9):642-50. doi:10.3967/bes2015.090.				X		
25.	Gao Y, Yan CH, Tian Y, et al. Prenatal exposure to mercury and neurobehavioral development of neonates in Zhoushan City, China. *Environ Res.* 2007;105(3):390-9. doi:10.1016/j.envres.2007.05.015.	X				X	

	Citation	Intervention/ Exposure	Age	Outcome	Study Design	Comparator	Publication Status
26.	Gari M, Grimalt JO, Torrent M, Sunyer J. Influence of socio-demographic and diet determinants on the levels of mercury in preschool children from a Mediterranean island. *Environ Pollut.* 2013;182:291-8. doi:10.1016/j.envpol.2013.07.022.	X			X		
27.	Gignac F, Romaguera D, Fernandez-Barres S, Phillipat C, et al. Maternal nut intake in pregnancy and child neuropsychological development up to 8 years old: a population-based cohort study in Spain. *Eur J Epidemiol.* 2019;34(7):661-673. doi:10.1007/s10654-019-00521-6.	X					
28.	Gispert-Llaurado M, Perez-Garcia M, Escribano J, et al. Fish consumption in mid-childhood and its relationship to neuropsychological outcomes measured in 7-9 year old children using a NUTRIMENTHE neuropsychological battery. *Clin Nutr.* 2016;35(6):1301-1307. doi:10.1016/j.clnu.2016.02.008.				X		
29.	Golding J, Gregory S, Ellis G, et al. Maternal prenatal external locus of control and reduced mathematical and science abilities in their offspring: A longitudinal birth cohort study. *Front Psychol.* 2019;10:194. doi:10.3389/fpsyg.2019.00194.	X				X	
30.	Golding J, Gregory S, Iles-Caven Y, Hibbeln J, Emond A, Taylor CM. Associations between prenatal mercury exposure and early child development in the ALSPAC study. *Neurotoxicology*. 2016;53:215-222. doi:10.1016/j.neuro.2016.02.006.					X	
31.	Golding J, Hibbeln JR, Gregory SM, Iles-Caven Y, Emond A, Taylor CM. Maternal prenatal blood mercury is not adversely associated with offspring IQ at 8 years provided the mother eats fish: A British prebirth cohort study. *Int J Hyg Environ Health*. 2017;220(7):1161-1167. doi:10.1016/j.ijheh.2017.07.004.	X				X	
32.	Groth E 3rd. Re: 'Maternal fish intake during pregnancy, blood mercury levels, and child cognition at age 3 years in a US cohort'. *Am J Epidemiol*. 2008;168(2):236. doi:10.1093/aje/kwn172.				X		

	Citation	Intervention/ Exposure	Age	Outcome	Study Design	Comparator	Publication Status
33.	Haapala EA, Eloranta AM, Venalainen T, et al. Diet quality and academic achievement: a prospective study among primary school children. *Eur J Nutr.* 2017;56(7):2299-2308. doi:10.1007/s00394-016-1270-5.	X					
34.	Halldorsson TI, Thorsdottir I, Meltzer HM, Strom M, Olsen SF. Dioxin-like activity in plasma among Danish pregnant women: dietary predictors, birth weight and infant development. *Environ Res.* 2009;109(1):22-8. doi:10.1016/j.envres.2008.08.011.	X				X	
35.	Hamazaki T, Hirayama S. The effect of docosahexaenoic acid-containing food administration on symptoms of attention-deficit/hyperactivity disorder-a placebo-controlled double-blind study. *Eur J Clin Nutr.* 2004; 58(5):838. doi:10.1038/sj.ejcn.1601888.				X		
36.	Handeland K, Skotheim S, Baste V, et al. The effects of fatty fish intake on adolescents' nutritional status and associations with attention performance: Results from the FINS-TEENS randomized controlled trial. *Nutr J.* 2018;17(1):30. doi:10.1186/s12937-018-0328-z.				X		
37.	Hart SL, Boylan LM, Carroll SR, et al. Brief report: newborn behavior differs with decosahexaenoic acid levels in breast milk. *J Pediatr Psychol.* 2006;31(2):221-6. doi:10.1093/jpepsy/jsj069.	X			X		
38.	Henriksen C, Haugholt K, Lindgren, M, et al. Improved cognitive development among preterm infants attributable to early supplementation of human milk with docosahexaenoic acid and arachidonic acid. *Pediatrics.* 2008;121(6):1137-45. doi:10.1542/peds.2007-1511.	X					
39.	Hertz-Picciotto I, Green PG, Delwiche L, Hansen R, Walker C, Pessah IN. Blood mercury concentrations in CHARGE Study children with and without autism. *Environ Health Perspect.* 2010;118(1):161-6. doi:10.1289/ehp.0900736.	X			X		

	Citation	Intervention/ Exposure	Age	Outcome	Study Design	Comparator	Publication Status
40.	Hibbeln JR, Davis JM. Considerations regarding neuropsychiatric nutritional requirements for intakes of omega-3 highly unsaturated fatty acids. *Prostaglandins Leukot Essent Fatty Acids.* 2009;81(2-3):179-86. doi:10.1016/j.plefa.2009.06.005.	X			X		
41.	Hibbeln J, Gregory S, Iles-Caven Y, Taylor CM, Emond A, Golding J. Total mercury exposure in early pregnancy has no adverse association with scholastic ability of the offspring particularly if the mother eats fish. *Environ Int.* 2018;116:108-115. doi:10.1016/j.envint.2018.03.024.	X				X	
42.	Hoerr J, Fogel J, Van Voorhees B. Ecological correlations of dietary food intake and mental health disorders. *J Epidemiol Glob Health.* 2017;7(1):81-89. doi:10.1016/j.jegh.2016.12.001.				X	X	
43.	Hsi HC, Jiang CB, Yang TH, Chien LC. The neurological effects of prenatal and postnatal mercury/methylmercury exposure on three-year-old children in Taiwan. *Chemosphere.* 2014;100:71-6. doi:10.1016/j.chemosphere.2013.12.068.	X			X		
44.	Iles-Caven Y, Golding J, Gregory S, Emond A, Taylor CM. Data relating to early child development in the Avon Longitudinal Study of Parents and Children (ALSPAC), their relationship with prenatal blood mercury and stratification by fish consumption. *Data Brief.* 2016;9:112-22. doi:10.1016/j.dib.2016.08.034.				X	X	
45.	Innis SM, Friesen RW. Essential n-3 fatty acids in pregnant women and early visual acuity maturation in term infants. *Am J Clin Nutr.* 2008;87(3):548-557. doi:10.1093/ajcn/87.3.548.	X					
46.	Jacobson JL, Jacobson SW. Prenatal exposure to polychlorinated biphenyls and attention at school age. *J Pediatr.* 2003;143(6):780-8. doi:10.1067/S0022-3476(03)00577-8.	X					

	Citation	Intervention/ Exposure	Age	Outcome	Study Design	Comparator	Publication Status
47.	Jedrychowski W, Perera F, Jankowski J, et al. Fish consumption in pregnancy, cord blood mercury level and cognitive and psychomotor development of infants followed over the first three years of life, Krakow epidemiologic study. *Environ Int.* 2007;33(8):1057-62. doi:10.1016/j.envint.2007.06.001.	X				X	
48.	Jensen TK, Grandjean P, Jorgensen EB, White RF, Debes F, Weihe P. Effects of breast feeding on neuropsychological development in a community with methylmercury exposure from seafood. *J Expo Anal Environ Epidemiol.* 2005;15(5):423-30. doi:10.1038/sj.jea.7500420.	X					
49.	Kim Y, Ha EH, Park H, et al. Prenatal mercury exposure, fish intake and neurocognitive development during first three years of life, Prospective cohort mothers and Children's environmental health (MOCEH) study. *Sci Total Environ.* 2018;615:1192-1198. doi:10.1016/j.scitotenv.2017.10.014.	X				X	
50.	Kishi R, Araki A, Minatoya M, et al. The Hokkaido Birth Cohort Study on Environment and Children's Health, cohort profile-updated 2017. *Environ Health Prev Med.* 2017;22(1):46. doi:10.1186/s12199-017-0654-3.	X					
51.	Lam HS, Fok TF, Ng PC. Long-term neurocognitive outcomes of children prenatally exposed to low-dose methylmercury. *Hong Kong Med J.* 2012;18(Suppl 6):S23-4.	X	X				
52.	Lauritzen L, Jorgensen MH, Olsen SF, Straarup EM, Michaelsen KF. Maternal fish oil supplementation in lactation, effect on developmental outcome in breast-fed infants. *Reprod Nutr Dev.* 2005;45(5):535-47. doi:10.1051/rnd:2005044.	X				X	
53.	Llop S, Ballester F, Murcia M, et al. Prenatal exposure to mercury and neuropsychological development in young children, the role of fish consumption. *Int J Epidemiol.* 2017;46(3):827-838. doi:10.1093/ije/dyw259.	X				X	

	Citation	Intervention/ Exposure	Age	Outcome	Study Design	Comparator	Publication Status
54.	Loring PA, Duffy LK, Murray MS. A risk-benefit analysis of wild fish consumption for various species in Alaska reveals shortcomings in data and monitoring needs. *Sci Total Environ.* 2010;408(20):4532-41. doi:10.1016/j.scitotenv.2010.07.013.				X		
55.	Lyall K, Munger KL, O'Reilly EJ, Santangelo SL, Ascherio A. Maternal dietary fat intake in association with autism spectrum disorders. *Am J Epidemiol.* 2013;178(2):209-20. doi:10.1093/aje/kws433.	X	X				
56.	Lynch ML, Huang LS, Cox C, et al. Varying coefficient function models to explore interactions between maternal nutritional status and prenatal methylmercury toxicity in the Seychelles Child Development Nutrition Study. *Environ Res* 2011;111(1):75-80. doi:10.1016/j.envres.2010.09.005.	X			X		
57.	Mamalakis G, Kiriakakis M, Tsibinos G, Kafatos A. Depression and adipose polyunsaturated fatty acids in an adolescent group. *Prostaglandins Leukot Essent Fatty Acids.* 2004;71(5):289-94. doi:10.1016/j.plefa.2004.04.002.	X					
58.	Marques RC, Abreu L, Bernardi JV, Dorea JG. Traditional living in the Amazon, Extended breastfeeding, fish consumption, mercury exposure and neurodevelopment. *Ann Hum Biol.* 2016;43(4):360-70. doi:10.1080/03014460.2016.1189962.	X					
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